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BIOSHIELD II: RESPONDING TO AN EVER-CHANGING THREAT

JOINT HEARING

BEFORE THE

COMMITTEE ON THE JUDICIARY

AND

COMMITTEE ON HEALTH, EDUCATION, LABOR, AND PENSIONS UNITED STATES SENATE

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WEDNESDAY, OCTOBER 6, 2004

UNITED STATES SENATE,
COMMITTEE ON THE JUDICIARY,
COMMITTEE ON HEALTH, EDUCATION, LABOR, AND PENSIONS,
Washington, D.C.

The committees met jointly, pursuant to notice, at 10:00 a.m., in Room 216, Hart Senate Office Building, Hon. Judd Gregg, Chairman of the Committee on Health, Education, Labor, and Pensions, presiding.

Present: Senators Gregg, Hatch, Enzi, Reed, Leahy, and Schumer.

OPENING STATEMENT OF HON. JUDD GREGG, A U.S. SENATOR FROM THE STATE OF NEW HAMPSHIRE

Chairman GREGG. I know we are going to be joined by a number of other colleagues. Unfortunately, at this time, there is a conference going on relatively to significant tax legislation which I suspect Senator Hatch is involved in. I am also involved in it relative to a number of issues, one of which is going to be taken up this morning, so I may have to leave to attend that conference, unfortunately.

But we did want to have this hearing today, this joint hearing today with the Judiciary Committee and the HELP Committee to address the issue of BioShield and how we are proceeding relative to the issue of bioterrorism and protecting our nation and our people against a bioterrorist attack.

Throughout the 1990s and the 1980s and certainly the 1970s and the 1950s and 1960s, when you discussed national defense and infrastructure for national defense, you always talked about whether or not we had the industrial complex to be able to maintain our capacity to defend ourselves as a nation. People talked about whether we could build planes or whether we could build tanks or whether we could build artillery and there was always a concern that our defense industrial complex might be eroding or was being shipped overseas.

Today, the defense industrial complex is entirely different because we are fighting a different war. The defense industrial complex, in other words, the industries which are going to defend us as a nation, are our technology industries and especially biologic industries. Our concern is that those industries which produce the medicines which will allow us to defend ourselves from an attack, a biological or chemical attack, those industries be vibrant, strong,

and robust in their ability to produce first the research, and then produce the anti-toxins and the vaccines necessary to protect our people.

That is why we passed BioShield. The whole concept behind BioShield was to create within the research community and those folks who produced biological agents which fight biological agents, vaccines specifically, produce an atmosphere where those companies, those individuals would have an incentive to go out and create the vaccines necessary to protect our people from attacks by biological agents, whether they be smallpox, anthrax, plague, botulism.

We recognize as a Congress that there isn't a consumer group out there that is going to use these types of vaccines other than the government, and therefore the government had to set up a system to try to create an incentive to produce these types of cures and vaccines.

The concern we have, I have, anyway, is that since BioShield has passed, we still have a very anemic response within the research communities and within the production communities to producing these types of vaccines and anti-toxins which would protect us in the case of an attack. Less than 100 companies have actually come forward and said that they have an interest in pursuing biologics.

So that creates a question. What else do we need to do?

What else do we need to do to make sure that there is an incentive out there amongst our creative and innovative people to produce the necessary vaccines to protect us as a nation from these types of biological attacks, because we recognize that in today's world, it is a biological or chemical attack, along with a potential dirty bomb, that is the most significant threat to us as a nation.

So that is what this hearing is about, to get an update on how people think BioShield I is working and to get some ideas as to what we should do should we pursue a BioShield II proposal.

I certainly appreciate Senator Hatch taking the lead in this effort with the Judiciary Committee and the HELP Committee working together. That is the type of cooperation that I think reflects well on us as a Congress, and certainly Senator Hatch has been a leader in all sorts of areas dealing with pharmaceuticals especially, having written the Hatch–Waxman Act, and was chairman of this, or ranking member on this committee for a number of years, the HELP Committee, and now, of course, runs the Judiciary Committee. So his knowledge on this issue is instrumental to our capacity to be successful as a Congress. So I will yield to my fellow chairman, Senator Hatch.

STATEMENT OF HON. ORRIN G. HATCH, A U.S. SENATOR FROM THE STATE OF UTAH

Chairman HATCH. Thank you, Mr. Chairman. I am grateful to be able to participate with you in this hearing because this is a very, very important hearing. We are both pulled all over Capitol Hill right now, so I am going to make my opening statement and then I am going to have to leave because I am in the middle of the conference on the Medicare, and you are also—on the FSC–ETI bill, excuse me, and that has been a very intense conference. But I understand Senator Enzi is going to be here, too.

Chairman GREGG. Senator Enzi is going to be here.

Chairman HATCH. That is great. You couldn't have anybody better. Let me just make these comments.

More than three years ago—now, I want to welcome our witnesses. They are great witnesses, great people to have here on both panels and I just want to tell you how impressed and how proud I am to have all of you here.

But let me just say, more than three years ago, our nation suffered the most deadly attack on its soil. We woke up on the morning of September 11, 2001, to a new reality. A month later, we again realized the magnitude of the ever-changing threat that we were facing when this building, this very building, was contaminated with anthrax and ended up being shut down for about three months. Most Americans were shaken out of their sense of complacency in 2001.

After the events of 9/11, Congress took action to secure our borders, our ports, and our airlines and bolster our public health infrastructure. However, the essential steps necessary to secure our nation against the ongoing threat of bioterrorism are still being carefully evaluated, and while these steps are being evaluated, time is running out.

We took an important first step when the Project BioShield Act of 2004, better known as BioShield, was signed into law in July. However, there is so much more that needs to be done. That is why the Judiciary Committee and the Senate HELP Committee are holding this hearing today, to raise awareness on what else needs to be done in order to combat bioterrorism.

I couldn't be more happy to work with a fellow chairman than with Senator Gregg. He has done a terrific job on the HELP Committee. It is a committee I have always taken a great interest in. I just admire him greatly. He is a very, very intelligent man who has done an awful lot of good in this body. So it is a privilege to be here with him.

It is common knowledge that terrorists are specifically interested in biological weapons. Many of these weapons were produced by Soviet scientists before the collapse of the Soviet Union and some experts believe that Soviet scientists concocted strains of smallpox that were 100 percent lethal. They developed a strain of yersenia pestis, the bacterium that causes the plague, which was resistant to ten types of antibiotics.

Today, it is unclear where many of these former Soviet scientists are working, and even more disturbing, it is not clear if these bioterror agents are still being kept in the former Soviet Union. As new varieties of bioterror weapons are developed, the threat of another attack becomes very real.

For this reason, I believe that the time for Congress to act on the Lieberman–Hatch–Gregg BioShield II legislation is now and I think it is important that we move ahead.

Even if we continue investing resources to build up a prepared public health infrastructure, if we do not have the medicines to treat those who are exposed or infected, the only other option is quarantining these individuals, and my colleagues, quarantining individuals, hundreds, maybe even thousands of people, will be extremely difficult to manage. So this is important stuff.

As I have said earlier, BioShield is only the first step to ensure readiness against this threat, and I am proud to say that the new law is based on legislation that my good friend and colleague, Senator Joe Lieberman, and I introduced this Congress, S. 666, the Biological, Chemical, and Radiological Weapons Countermeasures Research Act.

Today's hearing will focus on the next steps, essentially, what is needed in a BioShield II package and what we should do about it. BioShield II is the next step in the legislative process toward accomplishing this important and time-sensitive goal of bioterror readiness, and Senator Lieberman and I intend to reintroduce BioShield II legislation in the 109th Congress.

We simply cannot wait. Considering the anthrax attacks of 2001 and the ricin attack on our nation's capitol in February of this year, we already have ample reason to believe that the July law, while an important first step, is not sufficient and we need to move or to enact a more comprehensive legislative strategy.

Given the growing risk of further attacks on our nation and potentially devastating consequences of bioterrorism, we must abandon business as usual and take the vigorous steps that will be advocated through our BioShield II legislation.

The purpose of today's hearing is to expose and explore an array of intellectual property, liability, and other incentives to ensure the creation of a robust biodefense industry that needs to be included in the BioShield II legislation. Direct government funding for this research is not the most effective strategy. To be effective, we must also enact incentives so that potential investors will want to fund the research associated with building a defense against potential attacks. We must have the biopharma industry working with us on these solutions.

BioShield II will encourage biopharma companies to take the lead in the development of vaccines, therapeutics, and diagnostics to combat terrorism. The goal of our legislation is to have a safer and better prepared America, but in order to be prepared, we need to provide researchers with the proper incentives. These companies are worried about partnering with our government, and I believe Congress needs to engage the industry so that we can reap the benefits of their research. But forming partnerships with these companies is the key. Otherwise, this partnership will never work.

I look forward to hearing from our witnesses regarding this matter and what their thoughts are on what incentives should be offered to these researchers and companies.

Another critical question that will be explored today is whether these same incentives will apply to infectious diseases generally. In my opinion, all research on infectious diseases is interrelated, so we might strengthen bioterror research if the research focus is broader than just bioterror pathogens. Furthermore, by conducting this research, we may also discover cures for diseases that afflict the world's poorest nations.

I would like to acknowledge the terrific work of the HELP Committee, especially Chairman Judd Gregg and Senator Ted Kennedy, the HELP Committee's Ranking Minority Member, Senator Enzi, as well, but every member of that committee. I particularly appreciate you folks on that committee recognizing the importance of

this issue by agreeing to hold this joint hearing at such a busy time in the legislative session.

Majority Leader Frist has also been a leader in this area, and I want to thank the Judiciary Committee's Ranking Minority Member, Senator Pat Leahy, for his cooperation on holding today's hearing. Bioterrorism is an extremely personal issue for him. His office was one of the offices that received a letter containing anthrax.

Finally, I would like to recognize the work of our good friend, Senator Joe Lieberman, whose leadership on this issue has made the legislation possible and he deserves a lot of credit. I might add, he deserves credit for bringing this matter before our committees and the full Senate.

I also want to recognize the indefatigable efforts of Chuck Ludlam of Senator Lieberman's staff for his considerable efforts in developing this legislation.

Senator Lieberman is, of course, one of the managers of the intelligence reform bill which is pending on the floor this morning, and unfortunately, it is simply impossible for him to appear to present his testimony today. I ask unanimous consent that Senator Lieberman's testimony be included in the hearing record, and without objection, it will.

Senator Lieberman has asked me to send his apologizes to the committee and to all witnesses. We are all under a lot of pressure right now because it is the end of the session. I know Senator Gregg has a thousand things to do, and I am pulled all over Capitol Hill right now. I just have to say that, again, I appreciate all the witnesses that are going to be here today.

This is very important stuff, and I promise you that I am going to know everything that you say and I am going to pay very strict attention to it. I know all of your schedules are busy, too, and to join us today for this very important discussion is very important. So I look forward to hearing your thoughts and reading your thoughts on what should be included in our BioShield II legislation.

I ask unanimous consent that the following statements be submitted for the record. First, the statement of James Rafferty from Harkins Cunningham on tax incentives.

Second is the statement of George Barrett, President and CEO of Teva Pharmaceuticals.

And, of course, the statement of the Biotechnology Industry Organization. Without objection, we will put those in the record.

With that, I know Senator Leahy when he comes will have a statement, so maybe we could interrupt for Senator Leahy, or whoever is talking, when they finish, we can turn to Senator Leahy.

Chairman GREGG. You and I are probably going to have to leave in a few minutes to go to the FSC conference, and so I have asked Senator Enzi to chair the hearing and introduce the witnesses.

Chairman HATCH. That would be great.

Chairman GREGG. I will stay as long as I can.

Senator ENZI. Thank you, Mr. Chairman

Chairman Hatch. Thank you for doing this, Senator Enzi.

STATEMENT OF HON. MIKE ENZI, A U.S. SENATOR FROM THE STATE OF WYOMING

Senator ENZI. [Presiding.] I will also make some brief comments. I want to thank the chairmen, both chairmen, for this effort. This is very unusual for the United States Senate, to combine two committees, but it demonstrates the importance of this particular issue and the way that the two committees have worked together to handle the pieces of it that come under their jurisdiction.

The purpose of the hearing, of course, is to build a record. I think we have particularly capable witnesses today who will be building that record that the Senate can look at. We are doing this right now, even though it is the busiest time of the year for the United States Senate, so that we can have the jump on things when we get here next year, because that is when the action will be taken and this bill will have an opportunity to be one of the first in line.

Protecting America from bioterrorism will require the best efforts of both government and the private sector. This hearing today will demonstrate that. It will help us to see what more needs to be done to make America as safe as possible from this threat.

The legislation to enact President Bush's Project BioShield, which Congress passed into law in July, is an important first step towards securing our homeland and our citizens from a bioterror attack and its aftermath. I am proud to have cosponsored that legislation and I am committed to seeing the law improves our biodefense capabilities. My only regret is that it took more than a year for the full Senate to approve the bill after the HELP Committee reported it to the floor with unanimous support.

Now, looking forward, it is critical for these two committees to work together to build upon Project BioShield. Project BioShield was never intended to address all of the obstacles to the development of bioterror countermeasures. It was intended simply to establish a stable and guaranteed source of Federal financing for the purchase of countermeasures developed by private industry, since most of these products don't even have other significant commercial applications.

Now that we have established this financing mechanism, it is time that we address the other roadblocks that impede our progress on bioterrorism countermeasures. Chairman Hatch and Senator Lieberman have developed a bill that aims to address a wide variety of outstanding concerns that must be addressed, from liability protections to intellectual property incentives.

I was looking forward to hearing Senator Lieberman. I am very impressed with the testimony. I was anxious to see how he was going to condense that into just a few minutes. It is one of the most extensive testimonies that I have seen presented, and, of course, that becomes a part of the record today, as well.

I wholeheartedly agree with Senator Lieberman that we will not be able to address fully this threat without tapping the ingenuity that resides in these innovative industries. We need their input and involvement as we take the next steps toward protecting America from bioterrorism.

Again, I thank the chairmen and ranking members of both the committees, as well, for coming together to refocus these committees on our biodefense capabilities and I look forward to working

with the HELP Committee and the Judiciary Committee as we build this national biodefense.

[The prepared statement of Senator Enzi appears as a submission for the record.]

Senator ENZI. The panel that is before us, we have Christine Grant, who is Vice President of Government Relations with Aventis. It is the third-largest pharmaceutical company and one of the largest manufacturers of vaccines in the world. Aventis will provide their perspective on the remaining barriers to biodefense research and development.

We have Alan Timmins, who is the CEO of AVI BioPharma, which is developing treatments for a wide variety of infectious diseases and potential bioterror agents, including hepatitis C, West Nile, SARS, dengue fever, and ebola, to provide a smaller company's perspective on BioShield.

We have Kathleen Jaeger, the President and CEO of Generic Pharmaceutical Association. She will present the views of the generic pharmaceutical industry, and although generally supportive of including additional measures under BioShield, the Generic Pharmaceutical Association is concerned about some of the proposed patent and intellectual property provisions.

We have Carlos Angulo, who is with Zuckerman Spaeder. He represents the Coalition for a Competitive Pharmaceutical Market. It is made up of large employers, such as General Motors, Caterpillar, and of health insurers, such as Blue Cross–Blue Shield. The Coalition seeks to ensure the timely availability of lower-cost generic drugs.

We have Dr. John Bartlett, who is the Chief of the Division of Infectious Diseases at Johns Hopkins University School of Medicine. He is appearing on behalf of the Infectious Disease Society of America, IDSA. He will discuss why BioShield should be expanded to cover products intended to combat infectious disease generally.

We thank you for being here. Ms. Grant?

STATEMENT OF CHRISTINE GRANT, VICE PRESIDENT, PUBLIC POLICY AND GOVERNMENT RELATIONS, AVENTIS PASTEUR

Ms. GRANT. Good morning. Mr. Chairman, members of the committee, it is an honor for me to testify before you today about Project BioShield. I am here to represent one company, Aventis Pasteur. We are the largest company in the world devoted entirely to vaccine research, development, and manufacture. We produce more than a billion and a half doses of vaccine each year, protecting more than a half-a-billion people against 20 different diseases. We manufacture influenza vaccine and several other vaccines at our Swiftwater, Pennsylvania, plant here in the United States. We have had a variety of successes throughout the years.

And we have also been partnering with the Federal Government in times of peace as well as conflict. We provided support of tetanus and diphtheria vaccine after the attack on the World Trade Center. We donated 85 million doses of smallpox vaccine to the Federal Government. We have always supplied the U.S. military, including military needs today in the war in Iraq. And we have responded already to more than one Federal request for biodefense measures, and therefore, we have some current experience on the

subject. We have worked on global polio eradication and are actively involved in trying to develop a SARS and avian influenza vaccines.

We have testified in support of a number of the principles in BioShield I and we are pleased that you recognized in that bill that the development of medical and biological products requires a number of years under the most favorable circumstances to bring a product to market. That is why the multi-year contracting provisions were so important in BioShield I. We now ask and hope that HHS and the staff will implement those multi-year provisions enthusiastically as we now begin to see the fruits of BioShield I.

We also want to talk about the issue of having what are known as other transaction authority. Other transaction authority allows the HHS Secretary to contract with our biodefense companies for research, development, and manufacturing under one contract, under one roof. While the reports in BioShield I seem to indicate that other transaction authority was being provided, we would certainly encourage that that become explicitly considered in BioShield II. The reason is that, realistically, an established company like Aventis Pasteur not only does research and development, but we also emphasize the ongoing reliable manufacture of millions of doses of vaccine, so that when we have a satisfactory result at the research and development phase, we are in this business to continue to manufacture with HHS for HHS and the United States.

Similarly, Project BioShield I provided HHS the streamlined procurement authorities to ensure that contracting process is familiar, is consistent with commercial business practices, and that was a very important element. We now hope that HHS and its staff will have the energy, the enthusiasm, and the empowerment to ensure that it is not business as usual, but rather BioShield will be implemented in a way that is familiar to large established commercial companies.

Now, what remains to be done? Well, first, the issue of potential liability protection for entities such as us and other companies to get involved in this area is very, very important. For example, in our case, the absence of liability protection frankly was a major obstacle in our response to recent procurement by NIH for development of a next generation of anthrax vaccine. The absence of such liability protection continues to be a major hurdle for our company. We always try to obtain commercial insurance, but the practical reality today is that it is very unlikely to be able to obtain commercial insurance for projects of the nature contemplated by Project BioShield, and BioShield I was silent with respect to addressing liability.

Now, it is true that the passage of the Homeland Security Act of 2002 radically altered the way in which the U.S. can go about promoting the development of technologies. The Safety Act also provided some protections. But as you will hear in more detail from other witnesses, the Safety Act has not yet been applied essentially after the fact or for products such as vaccines, which are designed to protect against the eventuality of a terrorism attack, but rather it seems to be limited in practice to only actual terrorism attacks, and my written testimony suggests ways that we feel that one could argue that the Safety Act extends to vaccine.

Now, it is also worth noting that both the Secretary of HHS and DHS have already the authority to provide Federal indemnity to private contractors under Public Law 85–804. However, in our experience, use of such authority remains very, very rare. In March of 2003, President Bush revised Executive Order 10,789 governing the use of this authority to provide indemnity under Public Law 85–804 in the context of anti-terrorism technologies.

However, while HHS is currently using its authority in very limited circumstances, our problem in talking with HHS has been that the best understanding is that the agency is not providing such indemnification or other liability protection until, at best, a contract is awarded, and even then has not to date guaranteed that such protection will be forthcoming, even after an award is made. This, we are advised, has not been the same practice in other agencies and we would encourage working with you on that.

It puts us, as an established company, in the untenable position of having to perform a contract bare of liability protection and assume what are really very unusually high legal risks for these kind of projects. Once a contract is awarded, frankly, the leverage has changed. It is very difficult for us. We must rely on the agency to follow through and decide whether to provide liability protections.

So in summary, we would like to suggest that certainly going forward in BioShield II, that the authority for other transactions be offered and that we work together on liability protections, and I will be happy to answer any questions.

Senator ENZI. Thank you.

[The prepared statement of Ms. Grant appears as a submission for the record.]

Senator ENZI. My apologies to Senator Reed. I didn't notice that he was here until I had already introduced the first witness. I will interrupt so that he can do an opening statement. Senator Reed?

STATEMENT OF HON. JACK REED, A U.S. SENATOR FROM THE STATE OF RHODE ISLAND

Senator REED. Thank you very much, Mr. Chairman. We have a simultaneous hearing in the Armed Services Committee, so I will have to depart after my statement, but thank you.

Let me join my colleagues in commending the chairman and the ranking member of both the Judiciary Committee and the HELP Committee for holding this hearing and thank the panelists for their expert testimony.

This is a vitally important topic and I commend Senator Lieberman and Senator Hatch for their initiative in proposing their BioShield legislation. Since 9/11, we have taken dramatic steps in many different arenas, creating the Department of Homeland Security, conducting operations across the globe, in Afghanistan and Iraq, but I think we all agree we have to do much more when it comes to the threat of bioterror, chemical, and radiological countermeasures. The proposed legislation, I believe, is a step forward, following on BioShield I.

One of the concerns I have, however, with the proposed legislation is that it doesn't recognize the critical role that the government can play in directing, encouraging and generating some of the research necessary for this approach. We are all familiar with com-

mercial products that began through government research initiatives. The most famous is obviously the Internet, but satellites, explosive detection equipment, all these things started with government research and, frankly, government direction.

The private sector has to play a critical role here, but I would like to work with the sponsors of the bill to ensure that we take full advantage of the capacities of the Federal Government in this process.

One particular point that is critical when it comes to biotechnology and defenses against biological threats is that so much of this information is classified. So much of it is within the purview of the government because of its secrecy, because of the danger it poses if it gets out. So that, I think, is another element to consider.

Certainly, we have to be able to incentivize the private sector to produce these materials in a manner that is appropriate and have them in supply in case of a threat.

I look forward again to reading thoroughly all the testimony. Like Senator Enzi, I was hoping that Senator Lieberman would provide Cliff's Notes today for his extensive testimony—

[Laughter.]

Senator REED. —but I will read the testimony. I thank the panel and I thank the chairman for this time.

Senator ENZI. Thank you. I will mention to the panel that if you can condense your remarks to keep them within five minutes, as Senator Reed did, that it would be extremely helpful.

I will mention also that the record will be left open so that if you want to make some additions to your testimony, that will be possible, and also so that members of the committees can submit questions in writing, which we hope you will also answer to add to the record.

We will be kind of pressed for time today, because at 11:30, we start doing stacked votes, which will continue until the intelligence reform bill is finished, which could be very late tonight without any break. Normally, we would recess for a vote and come back, but that is not going to be a possibility today.

So with that, Mr. Timmins?

STATEMENT OF ALAN P. TIMMINS, PRESIDENT AND CHIEF OPERATING OFFICER, AVI BIOPHARMA, INC., PORTLAND, OREGON

Mr. TIMMINS. Thank you, Senator. Thank you for inviting me to testify today. I am Alan Timmins, the President and Chief Operating Officer of AVI BioPharma. AVI is an Oregon-based company that was founded in 1980 under the premise that the gene is the target for drug intervention. We have developed our own proprietary technology, distinct from that of other companies, and we have run 11 clinical trials serving over 300 patients without a single adverse event.

We have also found, though, that our technology is particularly germane in the area of infectious disease and specifically to bioterror threats. Particularly, it is available in a rapid-response format, and that is perhaps best illustrated by an incident that took place last February at the U.S. Army Medical Research Institute of Infectious Disease, USAMRIID, at Fort Detrick, Maryland,

where a post-doctorate researcher suffered a needle stick with a syringe that was filled with ebola. Now, Senator, as you know, ebola is a very lethal virus, and in fact, it is fatal in over 80 percent of the cases of people that contract it.

The researchers at USAMRIID called my company and asked if we were able to offer some sort of help. We looked at publicly available databases, found a couple of relevant genes, put together, synthesized a drug, helped USAMRIID get an emergency IMD from the FDA, and delivered the drug to USAMRIID all within five days of receiving that request. That gives you an idea of the power of the technology.

We also work in other infectious diseases, which we believe leads us to the ability to respond on a rapid response therapeutic basis to perhaps an engineered agent of bioterror, and that is important heading forward into the future. We also believe that we can address over 75 percent of the bioterror agents currently listed by the CDC.

But the issue here isn't the capability of my company or any other company, large or small. The issue here is whether or not we will be able to enact the principles laid down by Senators Lieberman and Hatch in BioShield II. I would like to comment very briefly on those particular premises.

In the area of tax incentives, a company like mine, a small company, we rely in a great degree on favorable capital markets to provide the funding to support our product development and to support the clinical trials necessary to get those products into the marketplace. The tax incentives sketched out by Senator Hatch and Senator Lieberman would be considered favorable by the capital markets, including the R&D partnership, which would allow usage of tax credits and business deductions on a timely basis, and also the capital gains incentive, which would encourage investment in smaller companies that are focused on biodefense.

Also important are the patent incentives, particularly the "wild card" patent incentive, which would allow for an extension of time for a relevant patent for a successful invention that is used in biodefense. That, along with a period of market exclusivity, is important also to investors in smaller companies that are developing biodefense mechanisms.

More important, though, than these two incentives are the liability protection that is spelled out by Senator Lieberman and Senator Hatch.

It is important that government gets back to being seen as a reliable, respectful, and responsible partner with industry and not in opposition to industry. The way that would happen is guarantees that intellectual property for companies, small companies, large companies, including patent protection, wouldn't be marched on or threatened by the government in the event of emergency. Rather, the government would work together in concert with the pharmaceutical industry and the biotechnological industry to bring the best biodefense mechanisms forward.

Without that sort of protection, I would submit to you, though, Senator, that you won't find the best companies, the best and the brightest, working toward biodefense. You will find them staying away from that because they will perceive that the threat to their

intellectual property is too great to take the risk to work with the government. That is unacceptable, in my opinion.

In conclusion, to address the threat of bioterror, to take a major step forward, there are four things that need to be done. First, we need to effectively enact the provisions of BioShield I.

Second, we need to provide appropriate tax incentives to foster investment in those companies that are going forward in biodefense.

Third, we need to look for patent incentives that help companies such as ours that are developing mechanisms to fight bioterrorism.

And fourth and most important, again, commit to liability protection. Commit to the government being a responsible and strong partner.

Senator I believe that those measures taken together would pay for themselves over a number of years. But most importantly, they will foster the innovative spirit of both the pharmaceutical industry and the biotech industry, and I would submit to you that that innovative spirit, when all is said and done, is going to be our most potent weapon in the war against bioterror.

I am willing to take your questions at any point. Thank you.

Senator ENZI. Thank you very much. Excellent job.

[The prepared statement of Mr. Timmins appears as a submission for the record.]

Senator ENZI. Ms. Jaeger?

STATEMENT OF KATHLEEN D. JAEGER, PRESIDENT AND CHIEF EXECUTIVE OFFICER, GENERIC PHARMACEUTICAL ASSOCIATION, ARLINGTON, VIRGINIA

Ms. JAEGER. Thank you. Chairman Gregg, Chairman Hatch, and Senator Enzi, I am Kathleen Jaeger, President and CEO of Generic Pharmaceutical Association. On behalf of GPhA and its members, thank you for this opportunity to testify on the ways to strengthen BioShield I.

GPhA and its member companies strongly support the stated policy goal of both BioShield I and S. 666, to ensure that America has the adequate supply of drugs and other products that would serve as countermeasures to bioterrorism attacks. Indeed, many of our members are already making substantial contributions to this end. However, new policies in this area must be balanced against the very real costs.

Mr. Chairman Congress took a significant step toward national preparedness with the passage of BioShield I this summer. We believe that the new law represents a sound foundation from which to build. As you know, BioShield I provided many of the tools needed to stimulate research and development of countermeasures. In many ways, Project I exemplifies what can result when the Federal legislative process works best by producing bipartisan legislation that utilizes a private-public partnership and research procurement and contracting to meet as major challenge head on. And already, we are seeing representatives of the pharmaceutical industry, the Federal Government, academia responding to the new laws, incentives, and call for action.

Nevertheless, even prior to enacting BioShield I, questions arose about the possible shortcomings, especially with respect to inad-

equate product liability protections. S. 666 is designed to address these concerns. Four notable provisions look particularly promising in this regard.

First, the limitation of product liability exposure to manufacturers of desired countermeasures.

Two, the provision of additional tax incentives to encourage investment in novel counter-bioterrorism products.

And third, the provision of FDA fast track review to expedite approval and availability of new countermeasures.

And fourth, additional Federal financial support for these initiatives.

However, we are alarmed that S. 666 includes provisions that reach into every medicine cabinet in America by effectively eliminating consumers' access to affordable generic products of everyday medicines. More specifically, the definition of what drug products would be eligible to receive an array of excessive and expensive incentives is extraordinarily, and we hope inadvertently, broad.

For example, the definitions could cover such ubiquitous pathogens as staph, E. coli, and other causes of common, everyday infections. While this may seem ridiculous, it could be shown that drugs widely used, such as Zoloft for depression, Plavix for heart attacks, Effexor XR for anxiety, Imitrex for migraines, could play a role in treating the symptoms of a bioterrorism attack and these would be eligible for additional protection under S. 666.

In addition, four provisions of S. 666, if allowed to stand, would unnecessarily and excessively penalize consumers to the tune of tens of billions of dollars in lost pharmaceutical savings. They would institute new loopholes that would extend additional and expensive market exclusivity provisions for brand products already on the market. Mr. Chairman these financial benefits would be on top of the other generous incentives already available.

As more fully detailed in our written testimony, these provisions, individually and collectively, will create devastating effects on the current health care system and undermine the balance of Hatch–Waxman amendments by, one, penalizing generic drug applicants with an additional five years of market exclusivity for merely filing applications as required by Federal law, and another five years if an applicant fails to successfully challenge a patent even though another generic company has prevailed and can bring their product to market.

Two, providing open-ended and unlimited patent extensions for all countermeasure drug products.

And three, needlessly extending current market exclusivities to ten years for something as simple as a conversion from a tablet to an extended release dosage form.

And four, granting a two-year wild card patent extension that can be applied to patents and products that are wholly unrelated to any countermeasure and which can be stacked one upon the other to indefinitely delay generic entry.

For example, under S. 666, a company like Pfizer could merely perform a small animal study on one of their commercially available antibiotics and that company could receive a windfall to extend the exclusivity of one of their blockbuster products for two years. Suppose Pfizer used its wild card on America's most rec-

ommended cholesterol-reducing drug, Lipitor. Pfizer's return would be a minimum of a $14 billion windfall.

Now, suppose that Pfizer performed a second animal study, either on the same antibiotic or on a different agent. They could claim that a $3 billion product, Zoloft, could get an additional two years of market exclusivity. And to that, again, there would be an additional $6 billion windfall, clearly to the detriment of patients and their families suffering from mental illness.

Mr. Chairman, as you can see, these four provisions taken to their logical conclusion could affect consumer access to and the affordability of most everyday medicines. All four of these provisions would inflate drug prices, impose major obstacles to the entry of generic drugs into the market, and worsen the crisis faced by every American who must pay for all or a substantial portion of his or her prescription drugs, including the millions of uninsured and older Americans. They serve little sound purpose, and unlike the other four positive provisions I earlier outlined, certainly would not strengthen BioShield I and better achieve its goals.

In conclusion, Mr. Chairman, the broad eligibility definitions and the excessive and unnecessary market protections of S. 666 give a blank check to PHRMA payable against the financial and health care interests of America, America's workers, businesses, and taxpayers. We think these provisions would be extraordinarily expensive and would do little to accelerate research and production of truly innovative products. Congress was right to reject, at least not include, such counterproductive policies when you passed BioShield I earlier this summer.

And lastly, GPhA and our members stand ready to provide whatever support we can to respond to your challenge to research, produce, and stock, and be ready to distribute new and effective bioterrorism countermeasures.

Thank you for the opportunity to testify. I would be happy to answer any questions.

Senator ENZI. Thank you.

[The prepared statement of Ms. Jaeger appears as a submission for the record.]

Senator ENZI. Mr. Angulo?

STATEMENT OF CARLOS ANGULO, PARTNER, ZUCKERMAN SPAEDER LLP, ON BEHALF OF THE COALITION FOR A COMPETITIVE PHARMACEUTICAL MARKET

Mr. ANGULO. Good morning, Senator Enzi. My name is Carlos Angulo and I am here to testify on behalf of CCPM, the Coalition for a Competitive Pharmaceutical Market, on S. 666, the BioShield II bill. Thank you for the opportunity to appear before you today.

CCPM is an organization of employers, insurers, generic drug manufacturers, and others committed to improving consumer access to affordable pharmaceuticals and promoting a vigorous, competitive prescription drug market. CCPM supports public policies that facilitate timely access to affordable pharmaceuticals. The Coalition, of course, is also absolutely committed to assisting Federal, State, and local governments and the American people in their efforts to develop quick, effective, and accessible responses to bioterrorism.

The Coalition's membership is broad, including numerous prominent purchasers of pharmaceuticals, such as General Motors Corporation, Caterpillar, Inc., and Eastman Kodak Company. On behalf of the Coalition, I would like to share with the committees today our experience regarding prescription drug cost increases and to underscore our belief that in its current form, S. 666 would dramatically delay generic drugs from coming to market and cause a crippling increase in prescription costs for America's employers, health plans, and consumers.

By way of background, large and small businesses, consumers, unions, governors, the Federal Government, and health plans throughout the nation are aggressively attempting to manage soaring prescription drug costs. These expenditures are growing at annual rates of up to 20 percent and are unsustainable. Current pharmaceutical cost trends are increasing premiums, raising copayments, pressuring reductions in benefits, and undermining the ability of businesses to compete. CCPM members seeking to continue to provide prescription drug coverage to employees and subscribers face a tremendous challenge in light of these skyrocketing pharmaceutical costs.

For example, General Motors, the largest private provider of health care coverage in the nation, insuring over 1.1 million workers, retirees, and their families, spent over $1.3 billion last year on prescription drugs. Despite GM's use of state-of-the-art management techniques that assure the most appropriate and cost-effective use of prescription drugs, its pharmaceutical bill continues to grow at a rate of 12 percent to 16 percent a year, more than quadrupling the general inflation rate.

Similarly, Eastman Kodak Company, which insures 150,000 covered lives, spends 31 percent of its health care dollars on prescription drugs. Kodak spent roughly $99 million on drugs in 2003 and its costs are growing each year.

The experience of insurers is no different. The 41 Blue Cross and Blue Shield plans that collectively provide health care coverage for 91 million Americans, represented in the Coalition by the Blue Cross and Blue Shield Association, are continuing to experience increases in prescription drug costs. The BCBS Federal Employee Program, for example, had drug increases over the last year of 9.67 percent. BCBSA expects these costs to continue to impact the affordability of premiums.

Such drug cost increases are driven by multiple factors, including higher utilization, direct-to-consumer advertisements, drug price increases, and especially delayed generic competition. If S. 666 passes in its current form, these costs will escalate dramatically and America will have a health care bill it cannot afford to pay.

The Coalition strongly supports legislation aimed at improving our ability to respond to terrorist uses of chemical or biological weapons. There can be no denying that the events of September 11 forever changed the way in which we work and we live. Today, we recognize that in order to protect our families, our friends, and our employees, we must be prepared for every type of situation.

For this reason, we wholly support the goals of the Project BioShield Act of 2004, or BioShield I, which went into effect just this summer. We also recognize that the effort to prepare our nation

against terrorist threats should include incentives to stimulate the development and production of drugs and other countermeasures, and therefore we support certain provision of S. 666, such as the provisions for tax credits, fast track Food and Drug Administration review of applications for countermeasures, protection against product liability suits, and the creation of a terror weapon countermeasures purchase fund.

It is also clear, however, that the goal of encouraging a response to bioterrorism must be balanced against the overall costs to American consumers and an already overburdened health care system. Unfortunately, as currently drafted, S. 666 has many unnecessary provisions that will increase costs without significantly benefitting the anti-terrorism effort. Specifically, there are four provisions in the legislation that would seriously hinder employers' ability to provide affordable health care to their employees and that would, in fact, deny public access to affordable versions of the countermeasure products that the bill seeks to make available to the American public.

First, S. 666's wild card exclusivity provision would give brand pharmaceutical companies a broad mandate to extend a patent for two years on virtually any drug they choose, even if it is completely unrelated to terrorism. This extension of brand company monopolies would force consumers and employers to pay billions of dollars in prescription drug costs beyond what they would pay if generic drugs were permitted to enter the market as provided under current law without significantly advancing any anti-terrorism goals.

Second, Section 5(f) of S. 666 expands by up to seven years the non-patent statutory exclusivity period for countermeasures. This change dramatically alters the careful policy balance struck by Congress under the 1984 Hatch–Waxman Act and last year's amendments to that legislation. S. 666 alters this balance by extending broadly, in certain cases by over 200 percent, brand company monopolies at the expense of consumer access to generic drugs.

Third, Section 5(c) of S. 666 would provide patent extensions for the full period taken to complete regulatory review for countermeasures. In certain cases, this provision would go so far as to reinstate patents on drugs that have been off-patent, forcing generic alternatives off the market. This bill would only exacerbate the problems of unsustainable health care costs and the growing number of uninsured Americans.

Fourth, Section 5(f) of S. 666 penalizes the generic industry for merely following the law in submitting generic applications with required patent certifications by providing that a generic company that submits such an application for a generic version must wait an additional five years for FDA approval beyond what is required under current law. This again contradicts the very intent of the Hatch–Waxman Act.

In short, and I will conclude, Senator, each of these four provisions of S. 666 standing alone could cost America's employers, insurers, and consumers billions of dollars without substantially assisting in the anti-terrorism cost. Each of these provisions has been rejected before by the Senate and by Congress. As innovators, patent holders and competitors in the world market, the Coalition

members respect the integrity and value of intellectual property protection, but not at the expense of consumer protections and lower drug prices for consumers and for our employees and retirees.

Thank you. I will be happy to answer any questions.

Senator ENZI. Thank you.

[The prepared statement of Mr. Angulo appears as a submission for the record.]

Senator ENZI. Dr. Bartlett?

STATEMENT OF JOHN G. BARTLETT, M.D., CHIEF, DIVISION OF INFECTIOUS DISEASES, JOHNS HOPKINS UNIVERSITY SCHOOL OF MEDICINE, ON BEHALF OF THE INFECTIOUS DISEASE SOCIETY OF AMERICA

Dr. BARTLETT. Thank you for the opportunity. I represent the Infectious Disease Society of America. It is an organization of about 7,000 or 8,000 physicians, most of whom do what I do, which is take care of patients with infectious disease.

I am here on behalf of the Society representing patients. We don't really have a commercial interest in anything. We are mostly worried about the availability of drugs in the event of a crisis, and we see an evolving crisis and that is the reason that we are particularly pleased to be invited.

The Institute of Medicine described the current era as a period in which there is a great probability of what they call a perfect microbial storm, and actually, there have been a bunch of them. SARS or avian flu or monkey pox or anthrax, any of these would be called potentially devastating infectious, especially if they hit the wrong place at the wrong time, and some already have.

What we are particularly worried about at the moment is the escalating problem of increasing resistance of the bacteria that we deal with every day, which is pretty predictable and it is shown on this visual here. The increase in some of the most common bacteria that we deal with every day in the hospital, we know that is happening because that has been an act of nature that we have dealt with ever since penicillin was brought on board in 1950.

But that is accompanied by a very distressing decrease in the number of antibiotics that we have available. So the number of antibiotics that we have is going down, down, down. In fact, in 2003, we had no new antibacterial agents introduced into the marketplace, which is really extraordinary.

Now, our Society has gone around and talked to ten of the major pharmaceutical manufacturers and we have done a lot of research in this area in terms of the pipeline and what we found is that many of the companies are either going out of business, and the rest of them that aren't going out of the antibiotic business are downsizing that operation. So when we look at the pipeline, for example, there are something like 503 new molecular entities in the pipeline, new drugs, and out of those, five are new antibacterial agents.

So when we look down the line, we see that miracles of the last 50 years, which have increased longevity by 30 years, is simply going to go away. So we are very worried about that problem of the dearth of antibiotics, new antibiotics, to deal with emerging crisis.

I did want to dispel a couple of what I think are common misperceptions. One misperception is that the NIH or other government agencies plays an important role in drug discovery. That is really not true. I expect everybody in this room has taken an antibiotic in the last ten years, took one that was discovered by a pharmaceutical company, developed by a pharmaceutical company, and brought to market by a pharmaceutical company. They have the history of having done it and certainly have the skill to do it.

Another misconception that is common is that we are actually not so bad right now, because if I have sinusitis, I can get a drug for it and it will take care of it. The fact is, we deal in an environment where we deal with serious infections that are very resistant. We are pulling drugs off the shelves that we haven't used in 20 years. Some of them are for this methicillin-resistant staph aureus that we are encountering very much more frequently and some of it is for this bug called acinetobacter, which is common in Iraq and now very common in the United States hospitals.

So we are worried about our ability to be able to keep up with the bugs at a time when the amount of available antibiotics is decreasing. And when you talk to the drug companies, it is very clear why they are going in this direction. You take an antibiotic for a week and you take Lipitor for the rest of your life. I mean, the economics are simple. It is not hard to figure out why they are doing what they are doing.

So I think what I would like to urge is in the framework of BioShield II, there be the possibility of responding to a microbial storm with the understanding that we don't know how that is going to appear. It might be a brand new bug, like SARS. It might be a really bad resistant bug, like acinetobacter. It might be a manufactured resistant organism, like anthrax. I am saying we don't know where it is going to come from, but we are pretty sure it is going to happen.

The other thing I would mention is that we now have to plan five to eight years down the line because that is the average time it takes to develop a new drug. So we are not talking about 2005, which is pretty bad in itself. We are talking about 2010. Thank you.

Senator ENZI. Thank you very much.

[The prepared statement of Dr. Bartlett appears as a submission for the record.]

Senator ENZI. This is a very impressive panel. One of the great perks of being in the United States Senate is the opportunity to learn about all these things that we probably wouldn't even have cared about before and some of the things that we never wanted to know about. It is a tremendous education. I think we probably pick up about a college course a month around here.

Again, we are under a little bit of a time constraint, so I do have a few questions that I want to ask right now. Hopefully, you will give me rather brief answers and expand on them later as you get other questions from us, as well. I know that several members of the panel wanted to ask questions based on the testimony that they received already and some that was presented today, so I will start with a few questions here.

Ms. Grant, BioShield provides no protection against the risk of litigation stemming from possible adverse events. How much of a risk does this present in the case of a biodefense product that is not required to undergo Phase 3 clinical trials, and in the event of emergency may not even be FDA approved?

Ms. GRANT. This is a very, very big risk, and in a sense, it is almost a non-starter because the realities of the commercial markets today here and around the world are that we just can't get commercial liability protection anywhere approaching reasonable prices. So it is a very, very serious problem. It has a chilling effect and our companies are watching very closely how liability protection will be addressed.

Senator ENZI. Again, on all of these questions, any of you that want to answer them, we will accept answers in writing on them, due to our limited amount of time.

Mr. Timmins, you run a small company based on the other side of the country. I am from Wyoming, and every business in Wyoming that is headquartered in Wyoming is a small business. I know that the Federal Government sometimes needs to be reminded that small companies don't know how to navigate Washington in the same way that big companies do. From your perspective, what does HHS need to do to ensure that small companies like yours understand how to work with the government on Project BioShield?

Mr. TIMMINS. Senator, that is a terrific question and probably one that should be the subject of a hearing in and of itself, because I can tell you, it is a hard running river and it is going in the wrong direction. You work your hardest. You try your best. But really, the key is to have terrific representation, as we are fortunate to in the State of Oregon and the people of the great State of Wyoming are, as well, great representation in the Senate offices so that the legislative assistants can help you navigate those waters. That has been our best help going forward.

And then we find, like Senator Gregg's staff, very helpful, just finding friends on, as we call it, a friendship tour, when we come back and talk to the various Senators and ask for their help, their assistance, what is the next step in the way as we are trying to get the message out.

Senator ENZI. Thank you. It sounds like a good topic for the Small Business Committee that I am also on, so we will pursue that.

Ms. Jaeger, you had that chart that was over there that I don't think is part of the record here. It was almost too small for me to be able to read from here. So if you would provide us with copies of that, I would really appreciate it.

For both you and Mr. Angulo, if you could provide us with some more detail on how those provisions might be revised that you mentioned that would place an extra constraint particularly on generic drugs, that would be helpful.

Ms. JAEGER. We would be pleased to.

Senator ENZI. Wording is always a difficulty around here, particularly if we don't have expertise in the area that we are working in—which does not stop us from working on something, but—

[Laughter.]

Mr. ANGULO. We would be glad to.

Ms. JAEGER. We would be happy to, Senator.

Senator ENZI. Again, we will have some additional questions for you, particularly concerning those specific points that you raised.

Dr. Bartlett, you called for a BioShield-like set of incentives to spur the development of new antibiotics. You specifically suggest that we need a guaranteed pool of money. However, you note in your testimony that there is a major civilian market for antibiotics. We don't have such a market for—although you made the distinction between Lipitor and antibiotics, as well, and then there is an even more limited market for bioterror countermeasures, which is why we created Project BioShield in the first place. Why would we need a guaranteed pool if we have a civilian market for antibiotics?

Dr. BARTLETT. Well, first of all, I think there are a couple parts of that. One is that if we have a major problem with a microbe such as the one I mentioned, acinetobacter, there is a big problem for us trying to take care of patients in the hospital. There is not enough of a market for any pharmaceutical company to ever develop a drug for acinetobacter. It will never happen.

The antibiotic market is between here and here. It is sinusitis and bronchitis and so forth. The other markets in medicine are much more profitable than the antibiotic market. So the civilian part of this is simply not going to go forward on the basis of what we perceive to be the biggest problems.

Senator ENZI. Thank you. I want to thank the entire panel and again encourage you to answer the questions that you will be receiving. Those answers will be a part of the record and will be shared with all of our colleagues.

While we are changing panels, the ranking member of the Judiciary Committee, Senator Leahy, can provide any statement that he wishes.

Senator LEAHY. My questions will be submitted for the record. I thank that all the panelists who have come here. Of course, we are in major debates on the Senate floor. This is probably the last week we will be in session until the lame duck. As the leaders, both Republican and Democratic, pointed out to all committee chairmen, this will be not a good week to hold hearings because nobody could be here. We are all, as I said, on the floor. So I just wanted you to know that it is not that we are not interested in what you have to say.

I also want to remark on how much has been left undone by the Senate. Some things, we don't get done. However, by law, we are required to pass a budget by April 30 and now, in October, there is no sign of it. By law, we are supposed to pass the 13 appropriations bills by September 30. We passed one. I guess somebody just pulled out a calendar and suddenly realized where we were.

So the empty chairs up here are not a sign of disrespect to you. I appreciate all of you being here, and I think you are going to have a lot of questions submitted. I am just going to give a short opening statement, Mr. Chairman.

Senator ENZI. We will have them stay there for a moment while you do your statement. Senator Schumer may be on his way down, too.

STATEMENT OF HON. PATRICK J. LEAHY, A U.S. SENATOR FROM THE STATE OF VERMONT

Senator LEAHY. The focus of today's joint hearing is an important one. That is why I wish it had been done during normal Senate time because it is an important one. I think in an increasingly uncertain world, the American people deserve assurance that government and industry are doing all they can to protect their health and well-being.

But this morning, that question is far from clear. As we meet here to discuss how to prepare our nation for the dire possibility of a catastrophic bioterrorist attack, the likes of which I hope we will never see, we learn that we are really not prepared to meet the biological threat that is here every year since I was born, and long before that. Of course, that is flu season.

I had hoped that the Bush administration would have learned their lesson from last year's experience, when we saw a major flu vaccine shortage. Now, we see health officials across the country, including in my home State of Vermont, asking healthy people just to forego their flu shot. I think the American people are right to challenge this vaccine rationing. They deserve an answer from the administration, why it didn't plan and prepare better. If they can't be prepared for the seasonal flu, which happens every single year, what does that say about the ability to prepare for biological terrorist attacks?

I will admit there is some interest in this. Like most people, I at one time or another in my life had a case of the flu. But unlike most people in this country, I have been the subject of a biological attack. There are two members of Congress, only two, that actually were threatened with a biological attack, Senator Daschle and myself. People who touched—touched—the envelope addressed to me, died. I think about the families of people who were crippled and stay crippled from that. I think of the people who died, simply because they were doing their job trying to deliver a letter to me. And, of course, my family and I think about what might have happened if I opened that letter. That was two of us up here. It could have been a whole lot more people. I am speaking, of course, of the anthrax attack.

But back to the flu, one of the primary problems with the flu vaccine that is highlighted by the administration's inability to deliver sufficient flu vaccines appears to be the concentration of producers. Market concentration is something the government can speak to. I believe the brand pharmaceutical industry is too concentrated. They fiercely lobby to extend their patents to prevent generic pharmaceuticals from giving consumers more affordable medicine. A huge amount of money is spent in this town for that.

Our constituents and, I think, members on both sides of the aisle need to ask why this country is so dependent on just two suppliers for this important vaccine. With all the pharmaceutical suppliers in this country, why is our government relying on a foreign supplier, which has now just been put out of business by the British government?

And so I would hope the big brand pharmaceutical companies would demonstrate their capability to respond to this crisis by answering the call of this flu vaccine problem rather than pushing for

patent extensions and windfall profits. It is probably too late this year, but they ought to be thinking about next year. I hope we can guarantee that neither I nor any other person in the government or in private industry will receive an anthrax attack like the deadly one I had, but we have to assume that 280 million Americans will be subject to getting the flu next year.

So I would hope we could address the potential crisis, make agreements to license and produce the vaccine the world needs. I would hope we would not find ourselves in this position again.

I will put into the record the rest of my statement. I am, among other things, pleased that the Congress took action to enact the Project BioShield Act of 2004. I applaud appropriately Senators on both sides of the aisle on that, and I will put that statement in the record. I know they will be eager to read it, Mr. Chairman as always, and I thank you for being here.

Senator ENZI. Thank you very much, and thank you for making your statement a part of the record since we are under the voting time constraint today where we have to start the series of votes at 11:30 and we have one more panel to go.

[The prepared statement of Senator Leahy appears as a submission for the record.]

Senator ENZI. With that, I will turn it over to Senator Schumer for a statement or questions.

STATEMENT OF HON. CHARLES E. SCHUMER, A U.S. SENATOR FROM THE STATE OF NEW YORK

Senator SCHUMER. Thank you, Mr. Chairman. I first want to thank both Senators Hatch and Gregg for calling this joint hearing about a very important homeland security issue.

There is no doubt that Project BioShield is an important piece of legislation and it provided a reasonable and needed incentive to encourage research and development of life-saving countermeasures to be used in the event of or to protect us from biological, chemical, nuclear attack, God forbid them all. We may need, though, to look at a few tweaks to make those incentives work like they were meant to work.

I understand that some of my colleagues may be drafting new bills. I look forward to seeing them. But I am deeply disturbed by the approach taken in a bill that is already out there which is identified as BioShield II. That is S. 666, and I am going to focus on that here today.

The bill contains patent provisions which undo almost every one of the important pro-consumer Hatch–Waxman reforms that my colleague, Chairman Gregg, and I fought so hard to have included in the Medicare bill. Its approach could indefinitely delay access to generic versions of all major blockbuster drugs and cost consumers billions—not millions, not hundreds of millions, billions of dollars.

To me, this amendment is, and I will restrain my language uncharacteristically, but it is awful, and it is taking a noble purpose and then sneaking in the wishes of the pharmaceutical industry that have nothing to do with protecting us from biological, chemical, or nuclear, and I will do everything to stop the entire bill if this provision stays in.

Let me describe it. The most egregious part of these patent windfalls is the so-called wild card patent extension. This provision says that if a company does research on a potential countermeasure, they would be rewarded with a two-year patent extension that they could slap on any drug they wanted. Do $20 million of research on one thing and get a $3 billion benefit on another. Who are we kidding? This is not intended to help biological research, which we desperately need. It is intended to give the drug companies even more.

I would hope that the people who put this in have learned their lesson. They tried to come up with a pharmaceutical bill, adding it into Medicare to help people. Do you hear President Bush talking about that bill in his election? Nope. Do you hear my Republican colleagues talking about that bill in their election? Nope. Why? Because they gave everything away to the big pharmaceutical industry. The idea that Medicare couldn't negotiate with the drug companies ruined the bill and it became a political albatross, and yet nobody seems to learn and we are doing the same thing right here.

Now, the bill says, you will say, the reward should only go to smaller drug companies, but it is the Secretary of Homeland Security's authority to waive this requirement, at least at the moment—maybe it will change—from the same administration that won't do anything—anything—that the pharmaceutical industry doesn't want.

One might think that in order for a company to get this reward, they would actually have to discover and produce a new life-saving, epidemic-stopping countermeasure, but that is far from the case. The company doesn't have to discover a new drug. They can do a test on one they are already marketing. They don't have to produce the drug for the government's stockpile. They don't even have to get the drug approved as a countermeasure and they can still get the multi-billion-dollar reward.

So the incentives in this bill make the American public pay billions of dollars to drug companies for no guaranteed return. No businessman would make that investment. Why are we?

Let me give you a sense of what this could mean for blockbuster drugs. Two extra years on Zocor, the popular cholesterol medicine, would mean a $9 billion windfall for Merck. Two extra years on Zyprexa, a drug used for schizophrenia, $6 billion for Lilly. Two extra years on Prevacid, blockbuster ulcer medicine, $8 billion for TAP Pharmaceuticals.

If we add up the value of just a one-year patent extension on the nine top drugs, just one year, nine top drugs, $31.5 billion, all to the pharmaceutical industry. That is more than the entire NIH budget, all of it completely allowed in S. 666, all of it with no return, no guaranteed return for the consumer.

The way I understand this provision, at least as it is drafted now, a company could get multiple wild card extensions and put them all on the same blockbuster drug, one after the other after the other. You could have these drugs or others, Lipitor or whatever, extended for years. This is Washington at its worst.

That is all I can say. I am infuriated by this. Let me ask the American people, do you think the only way that we can secure our

homeland is to pay tens of billions of dollars to the pharmaceutical industry? It is like ransom. We are not going to do it.

I would urge the people of this noble bill, and I certainly understand the need to give people incentives to invest in these things. I felt the same way when it comes to vaccinations and other things, you know, all the lawsuits and everything else that go too far, but this is not the way to do it.

With that, I would like to ask Mr. Angulo a question. Now, your Coalition represents some of the largest payers for health care in America, major employers, Kodak in my State, General Motors, which has a lot of employees in my State. What would be the impact of enacting the type of patent extensions described here today on the ability of these companies to provide quality health care for their employees at an affordable price?

Mr. ANGULO. The impact would be enormous and it would be enormously negative. Already, it is difficult enough under the current situation, the current landscape, to provide affordable health care to our employees, the Coalition's employees, the retirees, all the individuals that they are responsible for. To add this on top of it would, I think, create, as I said in my testimony, an unsustainable situation.

Senator SCHUMER. Thank you. My next question is for Ms. Jaeger. All of us agree that it is vital to enhance our medical defenses against deadly weapons of mass destruction, but we have to be careful to use our efforts wisely, our resources wisely. Aren't there more cost-effective ways to enhance the production of new vaccines and medication than providing wild card patent extensions that could cost billions of dollars every year? Isn't driving up the cost of prescriptions the last thing we should be doing right now?

Ms. JAEGER. Yes, Senator. We would agree that putting the burden on Americans who need medicine the most is not the right way of going and that really what should happen is that taxpayers should actually have to bear this burden equally among all.

And so, therefore, we would suggest that people consider full funding of these programs, perhaps providing more funding over to NIH and also doing very aggressive partnerships with private entities. We also think, again, another piece that would actually accelerate some development in this area is a product liability exemption for manufacturers.

So we think that the current environment, all the wonderful incentives that we provide to the pharmaceutical industry today, which include tax credits, market exclusivity, patent extensions, along with BioShield I and along with perhaps some other added concepts like product liability and additional tax credits, really would be the best way of going, and so that we can make sure that this nation is actually very secure and at the same time, we don't destroy our current health care environment, which is also in a crisis right now.

Senator SCHUMER. Thank you. Now, I have spoken strong language. If anybody would like, any of the other panelists would like to put in a counterword, I would like to hear what they have to say in defense of this specific provision. Does anyone want to defend it? No? Then my time has expired, Mr. Chairman. Thank you.

Let the record show no one wanted to defend it, at least on this panel.

Senator ENZI. Before the record shows that, while this panel is moving, I will make a comment on that.

Senator SCHUMER. Go ahead.

Senator ENZI. I do want the Senator from New York to realize that this is a bipartisan bill, and while all of the accusations went toward the Republicans on it, that one of the two drafters of this is from your side of the aisle. I think that there was a good bipartisan effort in coming up with this. Nobody said that it was a perfect bill at this point and there is a chance to work on it. I would provide a lot more rebuttal if we had more time, but we have another panel that we need to have and we are going to start voting at 11:30. Three people at five minutes doesn't get us done by 11:30.

Senator SCHUMER. I would just say, Mr. Chairman, my goal is to get this provision out of the bill, and whatever side of the aisle that comes from and whoever's side of the aisle put it in, it ought to be taken out right away. As I understand it, my colleague, Senator Kennedy, agrees with my thoughts on these issues.

Senator ENZI. And I did ask Ms. Jaeger and Mr. Angulo to provide us with some wording that would make that a more fair provision, but to keep in mind that we are trying to come up with some incentives for them to do these very short-term products. Dr. Bartlett gave an excellent explanation of the difference between Lipitor, which is for life, and antibiotics, which are for a week—

Senator SCHUMER. Mr. Chairman?

Senator ENZI. —and could have added this as being for the moment.

Senator SCHUMER. Right. Let me make the record clear. I am all for incentives to do this and I think you need them. I think no one in their right mind would want to give an incentive of $2 billion for a $10 million or $20 million—for an incentive that warranted a $10 or $20 million investment.

Senator ENZI. I understand that. I would also like to mention that the flu vaccine was mentioned, and I want to mention that Chiron was shut down by British regulators. I will be interested to see what that was. But the shortage does point out the need for new incentives and liability reform so that we aren't surprised by companies and so that we can have more companies in the United States who are involved in this process.

Our next panel is Mr. Jeff Kushan, who is a partner with the firm of Sidley, Austin, Brown and Wood, representing clients on a wide range of intellectual property matters, licensing, policy, and litigation.

Mr. John Clerici, who is a partner with the firm of McKenna, Long and Aldridge, with a focus on homeland security, particularly in the policy and legislative areas of how the government procures anti-terrorism technology from the private sector.

And Ms. Patricia Greenberg, a registered nurse who is the coordinator of the Nurse Alliance of New York State, which was established in September 2002. Ms. Greenberg has been a nurse since 1991 and has been a Service Employees International Union activist for over ten years.

Mr. Kushan?

STATEMENT OF JEFFREY P. KUSHAN, PARTNER, SIDLEY, AUSTIN, BROWN AND WOOD, LLP

Mr. KUSHAN. Thank you, Mr. Chairman, and thank you to all the other members of the committee for giving me this opportunity to testify before you today on the issue of market incentives to encourage development of countermeasures to respond to bioterrorism pathogens and threats. I am appearing today in response to an invitation to share my views on certain market exclusivity proposals contained in the Lieberman–Hatch bill. More importantly, I am testifying today in my personal capacity and the testimony that I am offering is my own.

During the deliberations that led to BioShield I, Congress appreciated the significant challenges in inducing the private sector to invent and bring to market new countermeasures to treat counterterror pathogens. The most significant of these challenges is there is no assured or consistent market for new products that might be developed. A company could thus spend millions of dollars, assume huge risks, only to find there is no market for its product or that that market is extremely limited.

Congress has partially addressed this challenge or this problem through its assured procurement opportunities and also by expediting the approval procedure for new products, but these measures are only going to go so far. Government procurement of products is both limited in its scale and subject to a number of risks that make this type of market opportunity less attractive than many other market opportunities that the biotech and pharmaceutical industry faces.

The true challenge of any legislative package is to convince the capital markets that the market opportunities associated with developing countermeasures are comparable to those for other types of drug development. A truly viable biodefense industry is one that will engage in new product discovery and development that is motivated by the opportunity for market success rather than by only through government subsidies.

As I note in my written testimony, the biotech and pharmaceutical industry markets are extremely market savvy. The industries are very market savvy, and more importantly, the markets are very savvy about the biotech industry. I tend to focus on the biotech industry because there is where you see most of the capacity for really high-risk innovative activity. Everybody is contributing to the environment, but those are the companies you really have to focus on inducing to shift their resources.

The formula that the market sees as necessary for success for a new venture is not only that a company has come up with a new product, but that it is going to have assured market exclusivity and meaningful market exclusivity once it finally reaches a market with that product. Meaningful market exclusivity in these industries means that the innovator will only face technology competition and not price competition for a reasonable period after it launches its product.

By technology competition, I mean you will see other products entering the market to treat that type of disease or disorder, but that you won't have intense intermediate price competition in other parties selling the same product. The inducement to technology

competition is what we are aiming for with incentive. We want more products, more approaches, more interventions, and that is what we have to figure out how to create.

Investors that participate in the biotech industry accept higher risks of failure because of the higher possible return on their investment, and that risk that they all tolerate is the risk of product failure. But they can't tolerate—and I deal with venture capital companies who evaluate opportunities and I deal with companies who have intellectual property that they are trying to get venture capital folks to give them money to support—they all focus on market exclusivity. They all want certainty. And they all want to have a finite number of risks that they face. What they can't face as a risk is the political uncertainty and other types of uncertainty that might destroy a market once they finally reach it with a new product.

The Lieberman–Hatch proposals that have been discussed before have some innovative approaches to tackling the challenge and creating significant and effective new incentives for developing countermeasures. I am going to talk about three of these briefly.

The first is the question of patent term restoration. There is currently an authority in the Hatch–Waxman Act for companies to obtain credit for the time they spend developing and getting their drugs through the FDA process. Under that equation, there is a partial credit system. You don't get the entire credit. This is something which should be solved or addressed in the system. Small companies that develop these products should be able to get the full period of exclusivity corresponding to the regulatory period.

The second issue is this patent bonus that has already been the subject of some discussion today, and I think this is a creative approach that Congress is grappling with. Certainly, there are a lot of variables in how you express it and pin it down, but fundamentally, it is an interesting concept that is similar to the pediatric exclusivity concept. Pediatric exclusivity is an option that if a company does pediatric clinical investigations, it can get six months of additional exclusivity. That mechanism has addressed a problem that the market hasn't been able to solve. The market is not going to encourage people to do clinical investigations in pediatric populations, so they had to come up with a broader incentive that addressed that market shortfall. The patent incentive that is being discussed here might do that by giving an alternate funding opportunity or an opportunity for return investment that is not there by the potential of the drug itself.

And finally, in the Lieberman–Hatch bill, there are a number of ideas for market exclusivity, data exclusivity, following approval of a new countermeasure. That would extend those periods out.

One point, and I will end on this. The one challenge for this entire class of products is that these products may never be used and the window of time following approval is fairly short, as was mentioned earlier, in some cases only three years after a product is approved for marketing. We might not have a need for using that product three years after a product is approved. And so some measure that will encompass out into the future and assure market exclusivity is warranted and I invite the members of Congress to

come up with the best type of package to induce this type of innovation. Thank you, Mr. Chairman.

Senator ENZI. Thank you.

[The prepared statement of Mr. Kushan appears as a submission for the record.]

Senator ENZI. Mr. Clerici?

STATEMENT OF JOHN M. CLERICI, PARTNER, McKENNA, LONG & ALDRIDGE, LLP, WASHINGTON, D.C.

Mr. CLERICI. Yes. Thank you, Senator Enzi. I want to thank Chairman Gregg, Chairman Hatch, Senator Kennedy, and Senator Leahy for taking on this issue, and most significantly, Senator Lieberman with Senator Hatch, who had the foresight to address this issue soon after the attacks of 2001 and bring the legislation to the forefront.

I also want to thank Secretary Thompson and Secretary Ridge. They have been on the forefront of implementing this legislation. Their offices have been open. Assistant Secretary Stu Simonson has been willing to work with industry to understand how this process should be implemented and he deserves credit for that openness.

Finally, I would like to applaud the passage of BioShield in this regard as a positive step in the right direction. The country is significantly safer because of the passage of BioShield and Congress and the administration deserve the credit for that.

The goal now is to build upon that success and address the major issues that are preventing biomedical countermeasures from coming to market.

Make no mistake, liability concerns are preventing biomedical countermeasures from entering the government's stockpile. We have worked in my capacity at the law firm with clients on the issue of product liability related to sales to the Federal Government. I helped with my firm and others on the passage of the SAFETY Act and its implementation, so I understand the provisions of that Act and how they apply to this market.

We also recognize that working on contracts for our clients, for SARS vaccine, for avian flu vaccine, for smallpox vaccine, for next-generation anthrax vaccine, for anthrax therapeutics, smallpox antivirals, botulism vaccines, and antidotes for ricin and cyanide, that these companies that are undertaking these efforts will get to a point where they will not sell to the Federal Government unless their shareholders are adequately protected on the liability issue. We have to recognize that this environment is in the post–Sarbanes–Oxley world and there are obligations that public companies have to mitigate these risks.

Currently, the threat derived from products in the countermeasures produced under BioShield are fundamentally different than the risks encountered by a typical drug company. They are meant to stop, to interdict, to prevent an unknowable criminal act of terrorism. The terrorists could engineer the toxin around the vaccine or around the countermeasure. The terrorist could use it in an entirely different way than we ever imagined. We have seen their creativity obviously three years ago to take no steps in that way.

We recognize that these products, by their very nature, can only be implemented and tested using an animal role. We can't expose healthy humans to these toxins. We have to rely on a lot of predictive models, on Phase 3 clinical trials, and a great deal of luck, and that is important to recognize that that threat is different.

As my co-panelist has already pointed out, these pharmaceutical drugs and biomedical countermeasures will be likely stockpiled for years. We are not sure where they are going to be deployed, or when they are going to be deployed, and we pray to God that they never are deployed. But they are sitting on the shelf to be administered by someone other than the pharmaceutical, other than the public health system maybe in the event of an emergency, and that risk is too great for companies to bear.

Currently, there are only two options to deal with this liability protection for the broad scope of biodefense countermeasures, Public Law 85–804, which was already touched upon by a prior witness, and the SAFETY Act. Public Law 85–804 has been used in the donation of smallpox vaccine by a couple of companies, and HHS has been willing to reach out and use that authority when it is necessary. But recognize that that authority still creates a litigation model. The government, if you will, acts as a super-insurer. It could be years before judgments are rendered and payments are made to compensated unintended victims of this act of terrorism.

And most importantly, as already has been pointed out, HHS will not negotiate these provisions in advance of award. Companies are faced to allocate scarce resources and use shareholder money for a contract that, if they win, they might not be able to accept because of the liability concerns, and that has happened, absolutely, since the year 2001.

The SAFETY Act, which again is a very powerful piece of legislation, is not a compensation act. It removes the liability as a matter of law and creates a presumption of dismissal from a lawsuit. It does apply to countermeasures that stop or prevent a terrorist attack, but it doesn't apply to the liability in its current form in the way it has been implemented for those dangers prior to the terrorist attack, such as those created by a vaccine with animal model testing and limited research and development.

And most importantly, HHS has not linked the SAFETY Act effectively to procurement. It is a two-step process. You get the award, you apply for the SAFETY Act. The uncertainty that these companies face cannot be passed to their shareholders as responsible corporate citizens.

The way to address this issue is to clarify the SAFETY Act to make clear that it does and can apply to liability that occurs prior to an act of terrorism, and I would urge you to also consider coupling the SAFETY Act with a compensation scheme. There is an effective compensation scheme already in law for smallpox vaccine under the Homeland Security Act of 2002 and the Smallpox Act of 2003 that Senator Gregg and Congressman Burr worked on. That measure could be easily extended to biomedical countermeasures and coupled with the SAFETY Act, the questions involving the concerns of the liability and whether or not that is adequate protection, coupled with the SAFETY Act, would certainly be an improvement over the status quo.

Finally, Mr. Chairman, I do comment in my testimony on antitrust provisions, as well. There are provisions in existing law that do not require Congressional action that Congress should urge the administration to use to discuss how this market can be better developed in the incentives that industry needs without fear of antitrust violations.

I am open to your questions. Thank you.

Senator ENZI. Thank you.

[The prepared statement of Mr. Clerici appears as a submission for the record.]

Senator ENZI. Ms. Greenberg?

STATEMENT OF PATRICIA B. GREENBERG, R.N., ON BEHALF OF THE SERVICE EMPLOYEES INTERNATIONAL UNION, AFL–CIO

Ms. GREENBERG. Good morning, Senator Enzi. My name is Patricia Greenberg and I have been a registered nurse since 1980, though I thank you for taking ten years off my age.

[Laughter.]

Ms. GREENBERG. I have worked in critical care, coronary care, intensive care, operating room, and neonatal intensive care. Currently, I am the Executive Director of the New York State Nurse Alliance of 1199 SEIU. On behalf of the Service Employees International Union, I thank you for this opportunity to testify.

I also want to thank the sponsors of S. 666 for honoring Kathy Nguyen. Kathy was a member of my local union who died from her exposure to anthrax.

SEIU is the nation's largest organization representing health care workers, with over half of our 1.7 million members made up of nurses, doctors, EMTs, and other occupations within the health care sector. Many of these employees work in occupations that would be defined as first responders in the event of a terrorist attack.

As nurses, we want to do everything in our power to respond to, treat, and care for any patient who may be a victim of a terrorist event. We have reviewed S. 666 and are supportive of the broad principles of the legislation, to encourage the development of new countermeasures to protect all of us from such threats.

In particular, we have noticed how S. 666 is quite comprehensive in protecting the drug and other biotech companies who produce countermeasures from liability. In sharp contrast, we are alarmed that there is no mention of providing protections for the front-line volunteers working to protect our national security if they suffer as a direct result of the implementation of any of these countermeasures.

Frankly, we have been down this road before. The Homeland Security Act of 2002 provided blanket liability protections for smallpox vaccine manufacturers, but no protections for front-line health care workers, their patients, or the public. S. 666 sadly mimics many of the same serious flaws contained in the Bush administration's failed smallpox vaccine program.

This bill is of even more concern when you consider that it is premised on the expectation that there will not be adequate time to do full safety testing on these newly developed measures. As a re-

sult, we fear that, once again, nurses and other first responders will be quite hesitant to roll up their sleeves to volunteer when they learn of the bill's deficiencies.

It is not right or even logical to go to great lengths to protect the manufacturers that create the countermeasures from liability and then ignore the safety needs of the first responders and their patients in the event of adverse reactions. I can assure you that the best countermeasures in the world will not be effective if health care workers and their patients do not have confidence in the safety of these countermeasures and if those injured can expect no more than a "get well" card from their elected leaders.

You may recall that in December of 2002, President Bush unveiled a smallpox vaccination plan to inoculate 500,000 health care workers within 30 days and ten million more public safety workers in six months. Six months prior to this announcement, a wide range of organizations told the CDC that the program would likely fail if serious gaps in patient and worker production were not addressed. We all know the result of that initiative. Today, less than one-half of one percent of the ultimate goal of ten million workers have been vaccinated in the program later called a fiasco in a Washington Post editorial.

I now that we can and must do better with S. 666. The example of the recent past points the way. Specifically, SEIU believes that the following nine elements must be included.

A requirement that first responders be educated about the risks and benefits of any new countermeasure before implementation.

A requirement that workers are free to decline newly produced vaccines or other countermeasures not sufficiently tested without fear of workplace discrimination.

Free and confidential medical screening for volunteering will be provided in any vaccine or drug trial to screen out those with preexisting medical conditions.

That patients be informed of the risks of any countermeasures that could impact their safety.

That the Federal Government will oversee the monitoring of any adverse effects in volunteers who receive countermeasures.

That any first responder volunteer who becomes ill due to any countermeasure does not face loss of income.

That free medical care be provided to those who volunteer if they become ill from any countermeasure.

That first responders be provided with an explanation of any new job duties resulting from the implementation of the countermeasures.

And, finally, contrary to how smallpox vaccine was administered, require that any new vaccines or other medications that utilize needles be administered with safe needles as required under the Needlestick Safety and Prevention Act of 2000.

I want to recognize and thank you, Senator Enzi, for sponsoring the Needlestick Safety Act. Thanks to this visionary action, there is no need for any tainted needlestick to ever threaten any health care worker again.

Thank you, and I would be glad to respond to any questions.

[The prepared statement of Ms. Greenberg appears as a submission for the record.]

Senator ENZI. Again, I want to thank this panel for some very detailed and useful information and critique of the bill. I wish we had some time for some extensive questions on it. We will be submitting questions to you in writing to get your response to make a part of the record, although the detailed comments that you gave are extremely useful.

I want to thank in their absence Senator Hatch and Senator Gregg and Senator Leahy and Senator Kennedy for holding this hearing. There was a lot of misgiving about what would happen with it when it was just prior to an election, particularly a Presidential election. I think, for the most part, we have avoided that kind of thing, because this is to get information for something that will begin after the first of the year but give our staff now something to really dig their teeth into and to get additional answers in response to your concerns and the concerns of the panelists.

One of the things that I have discovered around here is that we pretty much agree on about 80 percent of any bill. Unfortunately for America, it is the 20 percent that we don't agree on that we go to the floor and fight about, and that is one of the things that I have learned from working with Senator Kennedy on some of the things like the Needlestick bill, that when we work together, we can get some amazing things done. We will be watching out for the safety. That is why it is a joint committee on this.

We will be looking to see what incentives will work while best preserving competitiveness. I think that the testimony today shows the immense need for liability protection and worker protection.

With that, I will leave the record open and we will be getting questions to you to complete the record.

I would also like to include in the record the prepared statement of Senator Kennedy.

I thank everybody for their participation today. The hearing is adjourned.

[Whereupon, at 11:40 a.m., the committees were adjourned.]

[Questions and answers and submissions for the record follow.]

QUESTIONS AND ANSWERS

Responses of Carlos T. Angulo to Follow-Up Questions from Members of the Senate Judiciary and Senate HELP Committees Following the October 6, 2004 Hearing on S.666

A. Answers to Questions Posed by Senator Kennedy

Answer to Question #1:

Senator Kennedy, CCPM agrees with you that while the two-year wild card exclusivity in S.666 is a chief problem with the bill as currently drafted, it is certainly not the only provision of this bill that will have serious anti-competitive effects and thwart consumer access to affordable prescription drugs. Several other provisions of this bill, if enacted into law, would have similar consequences, providing windfalls to drug companies at the expense of health care coverage providers and consumers, without significantly aiding the anti-terrorism effort. One such provision is the provision in Section 5(c)(1) relating to patent term extensions for countermeasures.

CCPM applauds efforts to provide incentives to pharmaceutical companies to produce products that will assist our efforts against terrorism. Therefore, the Coalition supports the provisions in S.666 that would provide tax credits to manufacturers of countermeasures, protect these manufacturers from product liability litigation arising out of countermeasures, and provide for fast-track FDA review of new drug applications for such products. CCPM also strongly endorses the BioShield I legislation and urges that it be fully funded.

However, as set forth in CCPM's testimony, the process of determining appropriate incentives for the production of countermeasures cannot go forward without honest recognition of the costs of some of these incentives to employers and other health care coverage providers and the American public. The costs of providing health care coverage in America today is skyrocketing, increasing at annual and unsustainable rates of up to 20 percent. Extending for indeterminate periods patent protections for "countermeasures", a term which is defined so broadly as to include such commonly-used products as antidepressants and cardiovascular drugs with annual sales of over $1 billion per year, will cost America's businesses and consumers dearly - in many cases, without providing any incentive for brand companies to spend the money needed to develop *new products* that would be of use against bioterrorism. Given the already generous patent and exclusivity incentives that exist under the current patent law and the Hatch-Waxman Act, as well as the non-patent/exclusivity incentives contained in S.666, there is no justification for these additional patent incentives given their enormous costs.

In the end, CCPM believes that the single most effective manner of developing and facilitating public access to anti-terrorism "countermeasures" is by preserving a vital, competitive marketplace for these products, especially through broad public access to generic drugs. The patent extension provisions of S.666 are flagrantly anti-competitive and America and its citizens cannot afford them.

Answer to Question #2

The chief goal of S.666 should be to encourage drug companies to develop *novel and priority* products that could assist in our response to bioterrorism – not to reap additional monopoly profits from existing products that can be denominated "countermeasures" by virtue of a brief and relatively inexpensive animal study. Yet many of the provisions of S.666, including the patent extension provision discussed above, reward brand companies with patent and exclusivity extensions for products that are already on the market and as to which the additional studies required by the legislation are not particularly costly. In such cases, the costs of qualifying for the incentives of S.666 are dwarfed by the benefits received by the companies in the form of extended monopolies. Who are the losers in this equation? The businesses and consumers who are trying to keep up with upward-spiraling health care costs and who are denied the availability of generic alternatives to brand company products. The incentives in S.666 should be tied to the costs incurred by the drug companies the bill seeks to incentivize. Where the costs of qualification are low, the incentive merely provides a windfall to the drug company, at the expense of businesses and consumers. There is no justification for incentives under those circumstances.

Answer to Question #3

CCPM agrees that the definition of "countermeasure" in S.666 is extremely and unduly broad and, as applied in conjunction with the various patent and other exclusivity provisions of the bill, would confer enormous windfall profits on brand pharmaceutical companies. For example, a drug as simple and as available as aspirin could, by virtue of relatively inexpensive animal studies, be shown to be effective in treating the symptoms of bioterrorism. It could be argued, therefore, that the broad, anti-competitive intellectual property protections in S.666 would apply to the company that made this showing. As noted above, the purpose of S.666 should be to encourage the development of novel and priority products for use in the anti-terrorism effort, not to find new ways for brand companies to reap additional monopoly profits on products that have already been developed and approved, and that have been on the market and in routine use for years or even decades.

B. Answer to Question Posed by Senator Schumer

CCPM agrees that the "wild-card" exclusivity provision in S.666 is but one of several objectionable anti-competitive intellectual property provisions in the bill. Each of these provisions, standing alone, would cost America's providers of health care coverage and its consumers billions of dollars per year by extending brand drug company monopolies and, relatedly, by delaying or otherwise preventing public access to affordable generic drug products. Taken together, these provisions impose unsustainable costs on our health care system and in fact are antithetical to the goals of S.666, making it much more difficult for our citizens to gain access to the very same anti-terrorism treatments the bill seeks to make available.

In addition to the "wild-card" provision, CCPM has grave concerns with the following provisions of S.666, each of which benefits brand drug companies at the expense of health care

coverage providers and consumers, without proving significant assistance in the battle against bioterrorism:

Patent Extension Provisions: Section 5(c)(1) of S.666 extends patent protections for countermeasures in an amount equal to the full period of FDA's regulatory review of the relevant product. This provision eliminates the carefully-devised limitations on such regulatory review patent extensions that exist under current law. For example, under Hatch-Waxman, any patent extension based on regulatory review is limited to five years, and the overall patent term, when the extension is added to it, cannot exceed 14 years. S.666 eliminates these limitations, thereby permitting patent term extensions for countermeasures that are of indeterminate length. Moreover, under current law, there can only be one patent term extension per patent (even if the patent covers multiple products) and only one patent term extension per product (even one with multiple patents). S.666 also does away with these limitations for countermeasures. Finally, S.666's patent term extension provision even goes so far as to reinstate patent protections where the patent has already expired, which would have the effect of pushing already-available lower-priced generic substitutes off the shelves. In short, this provision will allow brand drug companies to extend their monopolies and to avoid for even greater periods competition from lower-priced generic substitutes, thus costing America's providers of health care coverage and its consumers billions of dollars per year.

Exclusivity Extensions: Section 5(f) of S.666 expands by up to seven years existing non-patent statutory exclusivity periods for those products denominated "countermeasures." Specifically, with respect to "countermeasures", the bill expands from five to 10 years the "new chemical entity" exclusivity; from three to 10 years the "new use" exclusivity; and from seven to 10 years the "orphan drug exclusivity." These exclusivity extensions dramatically alter the careful policy compromise struck by Congress under the 1984 Hatch-Waxman bill (and last year's amendments to that bill in the Medicare legislation), which sought to balance incentives for brand company innovation with increased public access to generic drugs. By expanding the statutory exclusivity periods, S.666 tilts the balance in favor of extended monopolies for brand companies and delays even further public access to affordable generic versions of the brand company product.

Anti-Generic Provisions: Finally, S.666 contains two "anti-generic" provisions which would delay further FDA approval of generic drug applications where the generic product was a substitute for a "countermeasure." The first of these provisions extends by five years a brand company's exclusivity period if it has a patent listed in the Orange Book. Because under the Hatch-Waxman Act, a generic company must certify to any such relevant patent as part of its application for FDA approval, this provision has the effect of adding five years of exclusivity whenever a generic application is filed certifying to a relevant brand company patent. Moreover, if the generic applicant certifies that the relevant Orange Book patent is invalid or uninfringed, and loses this challenge in court, the brand company gets an additional five years of exclusivity. In effect, these exclusivity provisions penalize generic companies for complying with their legal obligations to certify to brand company patents and create a significant disincentive for generic companies to challenge suspect brand company patents at all. As a consequence, these provisions once again extend brand company monopolies, reduce public access to affordable

generic products, and undermine the careful Hatch-Waxman balance struck by Congress two decades ago.

As if these provisions were not problematic enough in a vacuum, the broad definition of "countermeasure" makes them even more anti-competitive. As currently drafted, S.666 would award the various patent and non-patent exclusivity extensions even to brand companies that simply demonstrated that an existing product – even one as to which all relevant patents have expired – could be used as a countermeasure. In essence, all a brand company would have to do to reap billions of dollars of additional monopoly profits under S.666 would be to conduct some relatively inexpensive animal studies on an existing, already-approved product to demonstrate that the product could be used against bioterrorism. In certain cases where the relevant patents have expired, these patents would be reinstated, and any generic version of the product would have to be pulled from the shelves. Where the public already has access to a countermeasure at affordable prices, we gain nothing in the battle against terrorism by allowing brand companies to force their generic competitors off the market and to reap the enormous monopoly profits made possible by this bill.

In short, the intellectual property provisions of S.666 confer enormous benefits to brand drug companies in the form of expanded monopoly rights and delayed public access to affordable generic versions of brand company products. The impact of generic drugs on the health care cost bottom line cannot be overstated. The choice of a generic product over a brand product can result in savings of up to 70 to 80 percent, resulting in overall savings of $10 billion a year for consumers, employers, and insurers, as well as our state and federal governments. Thus, generic drugs play an indispensable role in the search for answers about how to decrease health care costs. However, the intellectual property provisions of S.666, as they are currently drafted, aggressively limit public access to generic drugs, at a cost of billions of dollars per year to consumers, employers, and others – while at the same time being of dubious benefit in the anti-terrorism effort.

Senator Schumer, you have asked CCPM whether there are other approaches to aiding the anti-terrorism effort that might be more cost-effective. Senator Enzi asked the same question at the October 6 hearing, and CCPM's response to your questions is set forth below.

CCPM would like to take this opportunity to reiterate that the Coalition supports efforts to encourage drug manufacturers to develop and market novel anti-terrorism "countermeasures." The question is, how can that be done while at the same time ensuring that the public will have access to affordable versions of these products and that health care costs can be kept under control. Many of the answers to this question can be found in S.666 itself, which contains, in addition to the objectionable provisions discussed above, a number of important provisions designed to encourage the development and production of "countermeasures." These provisions, which CCPM supports, include:

- Protections against product liability lawsuits;
- Tax credits;
- Fast-track FDA approval authority; and
- Creation of a Terror Weapon Countermeasures Purchase Fund.

In addition, *existing law* contains numerous patent and non-patent exclusivity provisions that encourage drug companies to expend the resources necessary to develop innovative new products. We believe that these provisions in current law in combination with the proposed non-intellectual property incentives in S.666 would provide ample inducements to brand companies to produce effective anti-terrorism "countermeasures," while at the same time preserving the public's access to these products through the maintenance of a healthy, competitive marketplace.

In closing, CCPM notes that the anti-competitive provisions of S.666 discussed above are not new proposals. Each of these provisions at one time or another has been considered by Congress, which has rightly concluded that each provision improperly and unnecessarily distorted the balance between encouraging innovation and containing health care costs. The Senate in its consideration of S.666 should reach precisely the same conclusion as it has in the past and reject these anti-competitive and counterproductive.

GPhA
GENERIC PHARMACEUTICAL ASSOCIATION

Responses to Written Questions
Senate Judiciary Committee
and
Senate Health, Education, Labor & Pensions Committee
October 6, 2004

"BioShield II: Responding to an Ever-Changing Threat"

Kathleen D. Jaeger

President & CEO

Generic Pharmaceutical Association

Questions Submitted by Senator Edward M. Kennedy

Joint Hearing before the Committee on the Judiciary and the Health, Education, Labor and Pensions Committee "Examining the Implications of Drug Importation" October 6, 2004

Question 1: *The 2-year wild card exclusivity in S. 666 obviously raises serious concerns, but there are a number of other aspects of S. 666 about which I also have serious concerns. That bill completely restores all patents on a countermeasure (with the exception of the one for which Hatch-Waxman restoration is given and the one for which the wild card exclusivity is given). This means that a countermeasure would have full patent protection for a period equal to the length of time from the date of issuance of the patent until it would have otherwise expired to begin on the date of FDA approval of the drug. An expired patent can apparently even be revived under this provision. This provision essentially means that a countermeasure will have at least 17 years of patent life. In addition, Hatch-Waxman data exclusivities of 3 and 5 years are extended to 10 years, as is the 7-year orphan exclusivity, if the countermeasure is an orphan drug. Finally, approval of a generic version of a countermeasure is delayed until 5 years after these restored patents expire.*

In other words, we are talking about at least a guaranteed 23 years of market monopoly for a countermeasure, and this does not even include pediatric exclusivity. Meanwhile, drug companies say that they get about 11 years of market exclusivity now. I understand the actual figure is closer to 14 to 15 years. If you use the drug company numbers, we are more than doubling market monopoly time. If you use the 14-15 year figure, we are increasing it by at least 50 percent. Whichever number you use, what are the costs to the American consumer and the health care system? Do these costs justify extending monopolies on countermeasures in this way?

As stated in our testimony, GPhA is concerned about preserving the balance between promoting the development and production of countermeasures and assuring the timely availability of affordable generic drugs. We strongly support targeted incentives that would lead to the development of innovative countermeasure drugs. However, we do not believe that our nation should be forced to sacrifice the timely availability of lower cost generic drugs in order to stimulate the development and production of pharmaceutical countermeasures.

The entry of generics makes the pharmaceutical marketplace more competitive, and the result of this competition is significant savings for consumers. From recent experience, we know that the average cost of generic drugs is about 70 percent less than that of brand drugs and that the annual savings to consumers from generic competition exceeds $10 billion.

As introduced, S. 666 would undermine those provisions of the Hatch-Waxman Act that promote the timely introduction of affordable generic drugs. The patent extension and market exclusivity provisions you cite would delay the entry of lower cost generics to the market for lengthy periods—and thereby defer the opportunity for consumers to save billions of dollars on their prescriptions for many years. The costs of these unwarranted exclusivity provisions would be borne by all those who have to purchase the drugs—including uninsured or underinsured consumers, as well as business and government purchasers of health benefits. This shift of costs is not only undesirable but also inequitable because it imposes these unnecessary added costs on those who are already struggling to cope with skyrocketing drug prices.

As GPhA has stated, we believe that more equitable incentives for developing pharmaceutical countermeasures can be found in the form of grants or tax incentives to manufacturers of countermeasures. That way, the nation as a whole—the ultimate beneficiary of the availability of countermeasures—equitably shares the costs. In addition, consumers and purchasers of health benefits would be spared unnecessarily inflated drug prices.

It is also important to recognize that many drugs likely to be deemed countermeasures under S. 666, such as antibiotics and other antimicrobials, have other more conventional uses in fighting diseases. Thus, extending monopoly protection or reviving expired patents would directly and unnecessarily inflate the cost of such everyday drugs.

Extending the monopolies on potential countermeasure drugs would be misguided public policy. It penalizes those who need these drugs for conventional medical treatment, and essentially puts the drugs out of reach for many of those without insurance coverage or the means to pay the higher prices for an unnecessary and burdensome period of time. Clearly, this undermines the intent of Hatch/Waxman and the core value of generic competition.

Question 2: *The extensions of market monopoly described in the previous question are available to compounds that have already been developed and may already be marketed as approved products. So all that needs to be done for these products—which everyone acknowledges will most likely be approved using only comparatively cheap animal studies, not the expensive human trials that are required for other drugs—is to spend perhaps as much as 20 million dollars to do an animal trial. And the company gets additional market exclusivities worth potentially billions of dollars. What is the argument that the immense value of the incentive is necessary, given the relatively modest cost of the research involved?*

GPhA believes that there is no valid reason to extend patents and market exclusivity for drugs that are already available and for which new uses as countermeasures might subsequently be established through relatively inexpensive animal trials. Extending market monopolies as an incentive is a grossly disproportionate reward for drugs which are already available and for which lower-price generic equivalents are now or will soon be available.

The innovator companies that make such drugs have already realized significant profits on these drugs through existing patent extensions, market exclusivity and tax credits. They already benefit from patent term restorations for time lost while testing a product and awaiting FDA approval (up to five years) and for delays in the Patent and Trademark Office (after three years). The Hatch Waxman Act also gives innovator companies between three and five years of market exclusivity, depending on the nature of the drug. There are additional provisions for orphan drug exclusivity (seven years) and pediatric exclusivity (six months). Moreover, generous tax provisions are available for general business research and development activities (tax credit of 20 percent of qualified spending above a base amount), orphan drugs (tax credit of 50 percent of the cost of human clinical trials), and activities in U.S. territories (exemption of 40 percent of the income from operations in Puerto Rico, the Virgin Islands, and other territories). The Uruguay Rounds Agreement extended patent terms from 17 to 20 years.

Thus, there is no need to provide additional rewards for brand companies. There may be some rationale for subsidizing some or all of the costs of additional trials to prove the applicability of these drugs as countermeasures, if only to ensure that adequate trials are conducted. But as your question suggests, these costs are likely to be relatively low, especially in relation to the continuing revenues that already accrue from the sales of these drugs.

Finally, there are numerous non-drug products that might be considered countermeasures, including duct tape, disinfectants, air filters and cleaners, and storm doors and windows. Yet no one is advocating that special market protections be extended to these products because of their potential use as countermeasures. For the same reason, one has to question the rationale for the extension of additional protections to drugs that are already approved and being marketed but for which countermeasure uses might be identified in the future.

Question 3: *The definition of countermeasure is so broad that it appears antidepressants and cardiovascular drugs with current annual sales of a billion dollars a year or more would be eligible for multiple year patent extensions. What is the justification for such windfall incentives, given the growing inability of our health care system, and of American patients, to withstand the constant increase in drug prices and drug utilization?*

We also are alarmed at the breadth of the definition of countermeasures in this proposed legislation. In its current iteration, countermeasures could include a wide range of conventional drugs such as antibiotics and other antimicrobials, pain medications, dermatological agents, anti-anxiety and gastrointestinal medications, vaccines, respiratory tract medications, anti-hypertensives and sedatives. In fact, the bill's definition of countermeasure might even encompass some drugs that are currently available over-the-counter without a prescription. The broad scope of the definition invites manipulation and abuse.

It would be preferable to focus the definition on truly innovative countermeasure drugs and devices. In many ways, the most effective targeted countermeasures are vaccines, laboratory diagnostic tools, and environmental detection/warning systems. GPhA supports direct public funding for such countermeasure products; this would place the burden of protecting our country on all Americans—not just those who need medicines, who would bear the full burden of increased costs from patent extensions and lengthened market exclusivity.

If a drug is already available—and, in particular, if a generic equivalent is already available—the notion of granting patent extensions is counter to sound health policy. Granting additional incentives and protections for drugs already available merely because one or more additional uses as countermeasures are fortuitously discovered or confirmed will grant unwarranted windfall profits to their manufacturers.

Particularly once a brand drug's patent expires, there is no reason to offer the manufacturer additional protections from competition merely because additional uses as countermeasures are subsequently discovered or validated. Such a step would destabilize drug markets and might even force the manufacturers of generics to withdraw the more affordable generics from the market merely because of the chance discovery of an additional use by the original patentee.

Offering added protections from competition for brand manufacturers in the form of lengthened patents or enhanced market exclusivity would represent movement in the wrong direction, sacrificing affordable medicine to promote the availability of countermeasures. Instead of this, Congress should maintain the system established under the Hatch-Waxman Act and strengthened last year by the Medicare Modernization

Act which assures that Americans have access to affordable drugs and select another approach to protect the country from bioterrorism and related threats. The optimal solution is one which builds on BioShield I, providing manufacturers of novel countermeasures with product liability protections, additional tax credits as well as direct subsidies, FDA fast track approvals, and upfront funding for smaller biotech companies.

We also are alarmed at the breadth of the definition of "covered activities" in this proposed legislation. As currently written, "covered activities" will include all the steps of the production chain of the countermeasures, including research and development, testing, production, distribution, and marketing. With this, brand manufacturers would have the functional equivalent of a merger for the purposes of the countermeasure. While we understand that certain incentives may be needed to bring brand manufacturers to the table, we do not believe that all the advantages of a merger are needed to make this possible.

It also appears that the brand manufacturers could benefit from the "fruits" of "covered activities," and those fruits could include secondary or tertiary products derived from exempted work on a countermeasure. In light of the fact that many pharmaceutical innovations happen by "accident," we strongly encourage the insertion of language making clear that the scope of any exemption is limited to the countermeasure itself, and does not apply to any "fruits" of the countermeasure, even if they grow out of exempted efforts.

Questions Submitted by Senator Charles E. Schumer
Hearing before the Committee on the Judiciary
and the Health, Education, Labor and Pensions Committee
"Examining the Implications of Drug Importation"
October 6, 2004

At the hearing, I expressed my strong opposition to the 2-year "wild card" patent extension provision in S. 666. However, this wild card patent extension is just one of the ways that consumer access to lower-cost generics is severely undermined by this bill. There are a whole host of other provisions that kick in when generics try to come to market with a lower-cost version of something that has been deemed to be a countermeasure.

First, the Hatch-Waxman law restores some of the patent time a brand company loses while a drug is going through clinical trials and FDA review—it restores up to 5 years. Under this bill, patent restoration would be unlimited for countermeasures. A patent can be expired by the time the company gets its drug approved and this bill appears to allow it to be "resurrected" for at least 17 years on the market. The way I read this provision, it could result in a generic actually being pulled from the market.

The bill also includes a data exclusivity provision—one which PhRMA has been most recently pushing through the back door at USTR—which would add a full 5 years before generics are even allowed to file applications to come onto the market.

Finally, the bill includes a provision which, in almost every case, when a generic does file an application there would be an automatic 5 year delay of generic approval. We just got rid of the multiple automatic 30-month stay which was given every time a generic challenged a new patent. This bill would institute a new, 5-year delay for every drug which could in some way be used after or to protect us from an attack. Even if a generic doesn't want to challenge the brand patents, even if the company files an application saying they're going to wait until all the patents expire, there would be an automatic 5-year delay.

In my view, these provisions not only have the potential to seriously delay access to generic versions of the countermeasures, but because the bill defines countermeasures so broadly, they could also easily apply to widely marketed drugs like antidepressants, blood pressure medicines, asthma medicines. These patent extension and exclusivity provisions could apply to any drug that could be used after or to protect us from a biological, chemical, or nuclear attack—whether it is a new drug or one that is currently marketed and has billions of dollars in annual sales.

What do you think the effect of these provisions might be on consumer access to generic drugs? In your view, what are some viable, more cost-effective, alternative approaches—or at the very least, modifications to the provisions included in the bill—which would encourage drug companies to research, develop, and actually produce needed,

life-saving countermeasures without causing such potentially devastating effects for consumer access to generic drugs?

GPhA strongly supports your opposition to the "wild card" patent extension provision in S. 666. Since the wild card incentive would be available for any drug in the product portfolio of the company manufacturing a countermeasure, regardless of whether that drug has uses as a countermeasure, the wild card provision is especially ill-advised and misdirected. As you point out, it would certainly undermine consumer access to affordable medicine.

GPhA believes that the current patent extensions, tax credits and market exclusivities granted under the Hatch-Waxman Act are sufficient compensation. Provisions are also already available for extending patents for delays experienced in the Patent and Trademark Office (PTO). Providing additional patent extensions and market exclusivities for countermeasures under S. 666 would be unnecessary and excessive. S. 666's approach would delay the availability of affordable generics, which would only weaken the health care system as a whole and injure those who are most dependent on affordable medicines—people who are ill and need access to drugs to treat their illness. Although generics represent about 51 percent of all prescriptions filled, they account for only 8 percent of total prescription drug expenditures. Extending patents and market exclusivity would clearly produce substantial price inflation as generics are kept from the market and consumers and purchasers of health benefits are forced to pay unwarranted monopolistic prices for many more years.

GPhA concurs with your interpretation that the patent extension provisions and increased market exclusivity could actually result in generics being removed from the market. This would seriously destabilize pharmaceutical markets and would reduce the access of countless consumers to more affordable generic drugs, with deleterious effects for their own individual health and the public health in general.

You are also correct in observing the inconsistency between those provisions of S. 666 which would further delay the entry of generics and the provisions of the Medicare Prescription Drug Improvement and Modernization Act of 2003, which eliminated multiple automatic 30-month stays that were granted when a generic manufacturer challenged a patent. The provisions of S. 666 which delay access to generics have no place in a bill whose purpose is promoting the availability of novel countermeasures. In keeping with the new Medicare law, we should be expanding—not restricting—the availability of generics.

We are also concerned that S. 666 defines countermeasures so broadly that there is a clear danger that many currently available drugs could be

considered countermeasures. These could include antidepressants, blood pressure medications, and asthma medications—as you point out—as well as a whole array of other drugs. Classification of such drugs as countermeasures under S. 666 would likely make them less affordable and less accessible to American consumers, as patents and market exclusivity periods are extended and the entry of generics to the market is postponed for years or even decades.

Regrettably, S. 666 has become a vehicle to achieve a set of patent extensions and enhanced market exclusivity provisions which PhRMA and its international affiliates have been aggressively pursuing for a number of years, attempting to use trade agreements and other means to extend product monopolies. PhRMA and its members have repeatedly attempted to extend market exclusivity to 10 years through trade agreements with Middle Eastern, Asian, and Latin American nations. PhRMA companies have also sought patent extensions or additional market exclusivity for a number of their individual brand products, including Claritin, Taxol, Ansaid, Lodine, and Toradol. S. 666 represents an attempt to accomplish in a single sweeping measure much of what PhRMA has previously tried to do in a number of discrete initiatives. Such an agenda should not be addressed in a bill concerned with promoting countermeasures.

As noted in our testimony, GPhA strongly supports BioShield I and those provisions of S. 666 which build on the intent of that law. Instead of erecting a set of incentives that would undermine the Hatch Waxman Act and limit the availability of generic pharmaceuticals, it would be preferable to take a more targeted approach, as was done in BioShield I. That is, the federal government should create incentives which are directly linked to the development and production of *new and innovative* countermeasures.

Because of the urgency of the need for an array of countermeasures, we need to marshal our limited resources and assure that they are not squandered on drugs that are already available. We need to embrace those options which are most directly linked to promoting the availability of countermeasure drugs and have the least possible negative spillover effect on our health care system, including any restriction on the availability of affordable generic drugs.

Logically, such an approach might include direct federal subsidies for research and development expenses as well as tax stimuli for such activities. "Fast track" FDA approval of new drugs developed as countermeasures is also desirable. In addition, steps should be taken to guarantee those companies that develop and manufacture countermeasures of a market for these products; this might include expanding national stockpiles and other measures to bolster procurement.

The nation also needs to take action to promote the availability of an adequate supply of diagnostics and environmental monitoring devices to help detect the presence of biological, chemical, and nuclear agents used for terrorist purposes.

In addition, there is special urgency to encourage the availability of new vaccines. The small biotech firms which have played such an important role in new drug discovery may need payments upfront to meet cash flow needs and subsidies to meet the costs of constructing new manufacturing facilities.

Finally, pharmaceutical manufacturers have valid reasons for concerns about potential liability, from the research and development stage up to and including actual production and distribution of countermeasure such as vaccines. This is one area where the federal government can intervene at relatively low cost to indemnify pharmaceutical manufacturers. The provisions of S. 666 for liability protection appear promising.

As introduced, however, S. 666 adds many benefits for the brand pharmaceutical industry at the expense of American consumers, taxpayers, and other prescription drug purchasers including the federal and state governments. The provisions that delay access to generics have no place in this bill, and would irreparably harm the American health care system. GPhA encourages Congress to amend S. 666 to provide real incentives to companies for the development and production of needed countermeasure drugs that are not currently available, while eliminating the "Christmas tree" of gifts sought by brand pharmaceutical manufacturers.

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November 11, 2004

BY HAND DELIVERY AND E-MAIL

The Honorable Orrin G. Hatch
Chairman, Committee on the Judiciary
United States Senate
Washington, D.C. 20510

The Honorable Edward M. Kennedy
Ranking Member, Committee on Health, Education, Labor and Pensions
United States Senate
Washington, D.C. 20510

Re: Joint Judiciary/HELP Hearing on Bioshield II

Dear Chairman Hatch and Senator Kennedy:

Thank you again for the opportunity to testify before the Joint Judiciary and HELP Committee hearing entitled "BioShield II: Responding to an Ever-Changing Threat" on October 6, 2004. Your continued, bi-partisan leadership on this critical homeland security issue is to be commended.

In response to Senator Kennedy's written question concerning the need for liability protections for companies that provide bio-defense countermeasures, I provide the following.

I agree completely with the suggestion of Senator Kennedy's question that any liability protections extended to companies that provide bio-defense countermeasures must be coupled with a complimentary mechanism to compensate patients injured by a faulty product. These concepts are not, in my view, mutually exclusive.

The first, co-equal objective must to provide liability protections that a provider of a countermeasure can feel certain will adequately protect the assets of the company and its shareholders. Such protections, in most instance, currently can be provided through certification under the SAFETY Act as provided in the Homeland Security Act of 2002. However, the SAFETY Act contains a "gap" that prevents manufactures of vaccines from being provided liability protection for injuries allegedly caused by the vaccine, itself, prior to a terrorist attack. Minor changes to the SAFETY Act can easily address this "gap" and carry out the intent of the law - that is, the broadest deployment of safe and effective anti-terrorism technologies, including bio-defense countermeasures.

The second, co-equal objective, must be to provide an adequate and reasonable compensation scheme to parties injured by an alleged failure of countermeasure to be effective against a biological, chemical, or nuclear terrorist attack, and/or for injuries alleged to be caused by the countermeasure itself. As you are aware, such a compensation regime currently exists under the Public Health Act for administration of the Smallpox vaccine. Minor changes to this existing legislative authority will serve to extend the coverage of this statute to any countermeasure administered as a result of a national emergency as declared by the Secretary of Health and Human Services. Limiting the trigger of this compensation regime to only those instance where the Secretary of Health Human Services has declared an emergency and directed administration of the countermeasure will have the effect of preventing these protections to be improperly extended to what are, in reality, not true countermeasures (e.g., ulcer treatments, etc.), as Senator Kennedy suggests is appropriate. Further, given that the SAFETY Act is limited only to "technologies" (in this case, countermeasures) that are deployed to prevent, protect against, or help in the recovery of an act of terrorist, the liability protections provided by the SAFETY Act would also be limited to not allow non-countermeasures to enjoy the benefits of this broad liability protection.

One issue that must be addressed both with the current Smallpox vaccine compensation scheme and any extension of this regime to other countermeasures is to ensure the compensation extends to all health care workers. There is some debate whether the protections afforded by the statute extend to health care workers otherwise covered by workers compensation or to injuries alleged to be caused by other than alleged negligence (i.e., strict liability, failure to warn, breach of warranty, etc.). Congress should take the opportunity when it extends these protections to all bio-defense countermeasures to ensure health care workers get the full protections afforded by the act as seems to be the intent of Congress.

I have attached proposed legislation that fulfills the objectives of providing the certainty of liability protections to providers of countermeasures and provides a mechanism for injured parties to be fairly compensated. I suggest this proposed legislation, or similar legislation, be strongly considered for inclusion in "Bioshield II" which I understand Senator Lieberman, Chairman Hatch, and Chairman Gregg intend to introduce in the 109th Congress.

I look forward to continue to work with you and your staffs to ensure these important public policy issues are addressed in future legislation. Please do not hesitate to contact me with any other questions.

Sincerely,

John M. Clerici

cc:

Chairman Judd Gregg
Senator Patrick Leahy
Senator Joseph Lieberman
Senator Mike Enzi

Proposed Liability Protection and Compensation Legislation for Countermeasures

(a) The Public Health Service Act Amendment. Section 224 of the Public Health Service Act (42 U.S.C. 233) is amended by—

(1) in the first sentence of subsection (a) by adding after "including the conduct of clinical studies or investigation" the words "or the manufacture or distribution of covered countermeasures as defined in subsection (p)".

(2) by changing the title of Section 224(p) from "Administration of Smallpox Countermeasures by Health Professionals" to "Administration, Manufacture and Distribution of Covered Countermeasures".

(3) in the first sentence of subsection (p)(1) by adding after "liability arising out of administration" the phrase "to an individual (including any and all individuals or entities involved with such administration), or the manufacture or distribution, including, but not limited to, by a health care worker or other person" and striking the words "against smallpox to an individual".

(4) by striking from the first line of subsection (p)(2) the words "countermeasure against smallpox" and inserting after the word

"concerning" the words "covered countermeasures, notwithstanding applicability of the SAFETY Act".

(5) in subsection (p)(2)(A)(i) by adding after "makes advisable" the designation "(i)", and after "categories of individuals" the phrase ",or (ii) the manufacture or distribution of a covered countermeasure for possible future administration to a category or categories of individuals".

(6) in subsection (p)(2)(A)(ii) by striking "(8)(A)" and replacing it with "(7)(A)" and adding after "administration to individuals" the phrase "(including any an dall individuals or entities involved with such administration), or for manufacturing or distribution, including, but not limited to, by a health care worker or other person".

(7) in the first line of section (p)(2)(B) by striking the word "only".

(8) in subsection (p)(2)(B)(i) by striking ", for a purpose stated in paragraph (7)(A)(i),".

(9) by creating a new subsection (p)(2)(D) as follows:

"Liability of United States for the Manufacture or Distribution of Covered Countermeasures.—Except as provided in paragraph 5(B)(ii), and notwithstanding the designation or certification of a

covered countermeasure as a qualified antiterrorism technology under the SAFETY Act (subtitle G of title VIII of the Homeland Security Act of 2002) the United States shall be liable under this subsection with respect to a claim arising out of the manufacture or distribution of a covered countermeasure, regardless of whether the cause action seeking compensation for the harm caused by such countermeasure is alleged as negligence, strict liability, breach of warranty, failure to warn, or otherwise, only if—

(i) the covered countermeasure was manufactured or distributed in accordance with, and during the effective period of, a declaration made pursuant to subparagraph A.

(10) in subsection (p)(4)(A) by adding after the words "arising out of the administration" the phase "(including any and all individuals or entities involved with such administration), or for manufacturing or distribution, including, but not limited to, by a health care worker or other person".

(11) by striking subsection (p)(7)A) and replacing it with the following:

(A) The term "covered countermeasure" shall mean a substance or product that is administered, manufactured or distributed in accordance with a declaration under paragraph 2 and that is–

(i) a drug or device subject to an emergency authorization pursuant to Part E, section 564 of the Federal Food, Drug, and Cosmetic Act;

(ii) a "qualified countermeasure" as defined in Section 121 of the Public Health Security and Bioterrorism Preparedness and Response Act of 2002 (42 U.S.C. 300hh-12); or

(iii) a "countermeasure" as defined by the Project Bioshield Act of 2004; or

(iv) used to prevent or treat smallpox (including vaccinia or another vaccine) or vaccinia immune globulin used to control or treat the adverse effects of vaccinia inoculation."

(b) The SAFETY Act (subtitle G of title VIII of the Homeland Security Act of 2002) is amended as follows--

(1) Section 863 (6 U.S.C. 442) is amended in each of subsections (a)(1), (a)(2), (d)(1), and (d)(2) by inserting after "from such act" the following: "or potential threat of such act".

(2) Section 864 (6 U.S.C. 443) is amended ---

(A) in each of subsections (a)(1), (b), and (c) by inserting after "from such act" the following: "or potential threat of such act"; and

(B) in subsection (a)(3) by inserting after "act of terrorism" the following: "or potential threat of such act".

(3) Section 865(1) (6 U.S.C. 444(1)) is amended—

(A) by inserting after "product" the following: "(including a vaccine, therapeutic or other biological, drug, or medical device)."

(B) by inserting after "information technology" the following: "or biotechnology or pharmacological product"; and

(C) by inserting after "preventing," the "treating,".

Responses to Senate Judiciary Questions
Christine Grant
Aventis Pasteur, Vice President, Public Policy and Government Relations
November 4, 2004

Questions for the Record
BioShield II: Responding to an Ever Changing Threat
Joint Judiciary/HELP Committee Hearing
October 6, 2004

Submitted by Senator Charles E. Schumer
QUESTION to Ms. Christine Grant

Question 1:

At the hearing, I expressed my strong opposition to the 2-year "wild card" patent extension provision in S. 666. However, this wild card patent extension is just one of the ways that consumer access to lower-cost generics is severely undermined by this bill. There are a whole host of other provisions that kick in when generics try to come to market with a lower-cost version of something that has been deemed to be a countermeasure.

First, the Hatch-Waxman law restores some of the patent time a brand company loses while a drug is going through clinical trials and FDA review-it restores up to 5 years. Under this bill, patent restoration would be unlimited for countermeasures. A patent can be expired by the time the company gets its drug approved and this bill appears to allow it to be "resurrected" for at least 17 years on the market. The way I read this provision, it could result in a generic actually being pulled from the market.

The bill also includes a data exclusivity provision -one which PhRMA has been most recently pushing through the back door at USTR -which would add a full 5 years before generics are even allowed to file applications to come onto the market.

Finally, the bill includes a provision which, in almost every case, when a generic does file an application there would be an automatic 5 year delay of generic approval. We just got rid of the

multiple automatic 30-month stay which w as given every time a generic challenged a new patent. This bill would institute anew, 5-year delay for every drug which could in some way be used after or to protect us from an attack. Even if a generic doesn't want to challenge the brand
patents, even if the company files an application saying they're going to wait until the all the
patents expire, there would be an automatic 5-year delay.

In my view, these provisions not only have the potential to seriously delay access to generic
versions of true countermeasures, but because the bill defines countermeasures so broadly, they could also easily apply to widely marketed drugs like antidepressants, blood pressure medicines, asthma medicines. These patent extension and exclusivity provisions could apply to any drug that could be used after or to protect us from a biological, chemical, or nuclear attack -whether it is a new drug or one that is currently marketed and has billions of dollars in annual sales.

What do you think the affect of these provisions might be on consumer access to generic drugs? In your view, what are some viable, more cost-effective, alternative approaches -or at the very least, modifications to the provisions included in the bill - which would encourage drug
companies to research, develop, and actually produce needed, life-saving countermeasures
without causing such potentially devastating effects for consumer access to generic drugs?

Response

While Aventis Pasteur strongly believes additional incentives are needed to stimulate the interest of established companies in the bio-defense market, and vaccines in particular, we have not recommended any single approach as to the best way to create such a stimulus. Specifically, as to the pharmaceutical patent issues to which you refer, Aventis Pasteur has not formulated a policy position.

As I noted in my testimony, the first obligation of the Federal government must be to remove all unnecessary barriers to entities participating in this market, first and foremost among them being the absence of liability protection and public compensation. Second, we need to ensure that the level of flexibility provided by Bioshield I in some areas of medical bio-defense procurement are embraced and implemented by the contracting agencies.

Questions for the Record
BioShield II: Responding to an Ever Changing Threat
Joint Judiciary/HELP Committee Hearing
October 6, 2004

Submitted by Senator Edward M. Kennedy
QUESTIONS to Ms. Christine Grant

Question 1:

The 2-year wild card exclusivity in S. 666 obviously raises serious concerns, but there are a number of other aspects of S. 666 about which I also have serious concerns. That bill completely restores all patents on a countermeasure (with the exception of the one for which Hatch-Waxman restoration is given and the one for which the wild card exclusivity is given). This means that a countermeasure would have full patent protection
for a period equal to the length of time from the date of issuance of the patent until it would have otherwise expired to begin on the date of FDA approval of the drug. An expired patent can apparently even be revived under this provision. This provision essentially means that a countermeasure will have at least 17 years of patent life. In addition, Hatch-Waxman data exclusivities of 3 and 5 years are extended to 10 years, as
is the 7-year orphan exclusivity, if the countermeasure is an orphan drug. Finally, approval of a generic version of a countermeasure is delayed until 5 years after these restored patents expire.

In other words, we are talking about at least a guaranteed 23 years of market monopoly for a countermeasure, and this does not even include pediatric exclusivity. Meanwhile, drug companies say that they get about 11 years of market exclusivity now. I understand that the actual figure is closer to 14 to 15 years. If you use the drug company numbers, we are more than doubling market monopoly time. If you use the 14-
15 year figure, we are increasing it by at least 50 percent. Whichever number you use, what are the costs to the American consumer and the health care system? Do these costs justify extending monopolies on countermeasures in this way?

Response to Question #1

While Aventis Pasteur strongly believes additional incentives are needed to stimulate greater private sect or interest in the bio-defense market, and vaccines in particular, we have not adopted any single approach as to the best way to create such a stimulus. Specifically, as to the pharmaceutical patent issues to which you refer, Aventis Pasteur has not formulated a policy position. We continue to believe that it is necessary to encourage the legislative debate

about how best to provide liability protections and public compensation for biodefense vaccines. Second, it is important to encourage the federal agencies to implement the initial procurement flexibilities provided in Bioshield I, or in the accompanying report language if established companies, already operating at near full capacity, are to be able to participate in this effort.

As you know, Aventis Pasteur is in the business of developing and manufacturing vaccines. Vaccines are usually complex multiple component biological products and most have only limited manufacturing process patent protection. Indeed, vaccines are biologicals, and to date, biologicals have not been accorded exclusivity under Title 1 of the Hatch-Waxman Act . Vaccines would rarely qualify for Orphan Drug Act designation, since all FDA licensed vaccines for protection against infectious diseases are administered to over 200,000 individuals annually in the U.S. and are thereby excluded from designation under current FDA regulations. Between 1990 and 1998, only four FDA-licensed vaccines have received patent term restorations under Title II of the Hatch-Waxman Act. The average patent extension received for these vaccines was 4.1 years and their average effective patent life even with those extensions was only 10.25 years. This is significantly shorter than either the 17-year or 20-year patent terms associated with earlier U.S. law or current U.S. and EU guidelines. Three of these vaccines are no longer licensed or being produced for use in the U.S. (two DTaP vaccines and one rotavirus vaccine). The only one of these vaccines still on the U.S. market received only a 2-year patent extension, since it required 17 years after its patent issuance date to gain FDA licensure. Vaccines have not enjoyed the patent terms and other intellectual protections referred to in your question. It is therefore reasonable to have a legislative discussion to consider the extent to which patent term extensions and other forms of intellectual property protection will be needed to stimulate the development of new preventative or therapeutic biodefense vaccines.

As I noted in my testimony regarding approaches to engage an established company in biodefense vaccines, the first goal of the Federal government should be to remove all unnecessary barriers to entities participating in this market. First and foremost among these barriers is the absence of effective liability protection and public compensation for biodefense vaccines. Second, there is a critical need to strengthen similar protections and compensation programs applicable to other vaccines to stabilize the broader vaccine enterprise. Third, current interpret ations of the revenue recognition guidelines of the Securities and Exchange Commission are impeding the efforts of the Centers for Disease Control and the Department of Health and Human Services to establish and maintain critical emergency stockpiles of children's vaccines, biodefense vaccines and other medical countermeasures to protect our nation. It is critical that this problem to be addressed either by the affected federal agencies, or if necessary, by legislation.

Question 2:

The extensions of market monopoly described in the previous question are available to compounds that have already been developed and may already be marketed
as approved products. So all that needs to be done for these products-which every one
acknowledges will most likely be approved using only comparatively cheap animal studies, not the expensive human trials that are required for other drugs-is to spend perhaps as much as 20 million dollars to do an animal trial. And the company gets additional market exclusivities worth potentially billions of dollars. What is the argument that the immense value of the incentive is necessary, given the relatively modest cost of the research involved?

Response to question #2

Again, as to the pharmaceutical patent issues to which you refer, Aventis Pasteur has not formulated a policy position. However, the costs of research, development, manufacturing and licensing of a new vaccine, whether for civilian public use or biodefense, are vastly higher than the estimates cited in your question. Various federal agencies have discussed the utility of animal models. However, the actual type and nature of the animal efficacy studies, and the size of the safety and immunogenicity studies in humans that will that be necessary and sufficient to obtain an FDA license for a biodefense vaccine, remain unclear. It is also likely that if FDA licensure is predicated solely on the use of animal models then extensive post-licensing studies will need to occur in humans.

The committee should recognize the cost of development and licensure of human vaccines are not trivial. For example, the developers and manufacturers of the intranasal live attenuated influenza vaccine, FluMist™, have reported that they invested over $1 billion in this product and facilities before they sold the first dose of the vaccine last year. Additional trials are still being required for the vaccine to obtain additional indications for use. Obviously, it will take that company a long time to recoup their investment (if ever) given the limit ed number of doses they have sold to date.

To date, reported data regarding the costs of developing and manufacturing biodefense vaccines are limited in scope, but several cases are well documented. For example, the Department of Health and Human Services and vaccine company contractors have obligated in excess of $500 million on the development and acquisition of new vaccines against smallpox, which have yet to be licensed, by the FDA. Thus far, the Department has also obligated over

$200 million on the early stage development of two recombinant anthrax vaccine candidates requiring the animal efficacy testing referred to in your question. Consequently, it is premature to conclude that biodefense vaccines will be less costly than other vaccines to produce, license and conduct post-licensure trials.

Question 3:

The definition of countermeasure is so broad that it appears antidepressants and cardiovascular drugs with current annual sales of a billion dollars a year or more would be eligible for multiple year patent extensions. What is the justification for such windfalls incentives, given the growing inability of our health care system, and of American patients, to withstand the constant increases in drug prices and drug utilization?

Response to Question #3

Specifically, as to the pharmaceutical patent issues to which you refer, Aventis Pasteur has not formulated a policy position. We hope that the information we provided in our response to the question is useful in highlighting the current situation with respect to patent and other forms of intellectual property protection for vaccines.

As I noted in my testimony and in our responses to your other questions above, the first obligation of the Federal government should be to remove all unnecessary barriers to entities participating in this market, first and foremost among them being the absence of effective liability protection and public compensation for both biodefense vaccines and for those for the protection of Americans from other infectious diseases.

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November 12, 2004

The Honorable Senator Orrin G. Hatch
Chairman
Senate Judiciary Committee
224 Dirksen Senate Office Building
Washington, D.C. 20510

ATTN: Barr Huefner

Dear Senator Hatch:

I wish to thank you and Senator Gregg, and the Members of the Committees on the Judiciary and on Health, Education, Labor and Pensions, for giving me an opportunity to provide my personal views on the intellectual property provisions of S.666 (Bioshield II).

As I indicated in my testimony and in the hearing, I was asked to testify in my personal capacity on certain provisions of the Bioshield II legislation. I am a practicing patent lawyer, and work with a wide variety of patent-dependent companies, particularly those in the biotechnology, pharmaceutical, and software industries. I drew from my experiences as a patent lawyer in preparing and delivering my testimony to the Committees. In particular, I sought in my testimony to explain to the Committees my view that the measures that were included in Bioshield I are positive, but, standing alone, would be unlikely to cause the private sector to shift resources (financial and otherwise) to conduct research and development to identify and bring to market new countermeasures to biological terror agents. I also indicated my belief that the existing commercial development environment for biotechnology and pharmaceutical products, including as established by the Bioshield I legislation, does not provide a significant stimulus for companies to engage in such research and development efforts.

Let me again stress that my testimony then and the answers I am providing through this communication are my personal opinions. During the hearing and in some press contacts I have had since the hearing, it has been suggested that the views I offered were on behalf of a client. This is not the case. My views, expressed then and now, are my own. They are based on my experiences in working with small and large companies trying to develop new products and from working with venture capital funds and other entities that are partnering with these companies. I

also base my views on my experiences inside and out of the United States government, where I had the opportunity of working on legislation and other sources of patent policy.

At the hearing, I testified that the market incentives that exist today generally do not induce biotechnology or pharmaceutical companies to undertake development of countermeasures. I observed that some progress has been made through the assured procurement authority of Bioshield I. However, I also observed that competition is fierce for limited sources of private capital to invest in research and development of new biotech and pharmaceutical products. For example, I noted that countermeasures, once developed, may never be purchased, or may be purchased on terms that do not provide a strong economic reward for the developer of the countermeasure. I believe that is the reality of the market today, and that unless other mechanisms are created, limited market demand will cause few companies to invest in development of countermeasures – particularly at the expense of development of other types of healthcare products.

Your letter presents two questions from Senator Kennedy. The first question is:

> You say that wildcard patent extensions are analogous to the system of rewarding drugs for pediatric indications with six months of extra exclusivity. Isn't it the case that the pediatric exclusivity applies only to the drug that is being developed for children – not to whatever blockbuster drug the company selects?

In my testimony, I indicated that the patent bonus concept was analogous to the system of pediatric extensions for pharmaceutical products. The basis for my opinion was that pediatric exclusivity – like the patent incentive for countermeasures for bioterror agents – creates a *general* economic incentive that is *not proportional* to the actual market opportunity associated with the *pediatric* sales of the product. Except in rare cases, the pediatric population for a drug product will be a small, and often tiny, fraction of the overall market for the drug. Revenue from sales to this small fraction of the market will be limited – meaning that there is not much of an economic incentive for a company to do the clinical testing of the drug necessary to permit pediatric sales, given the significant cost and difficulty of doing such testing. In return, however, a pediatric extension provides the pioneer manufacturer with six additional months of *general* market exclusivity, during which only that manufacturer can sell the product. The pediatric market exclusivity thus does not give rights only with respect to sales to the pediatric segment of the market for the drug. Instead, it gives the pioneer manufacturer an economic benefit from exclusive sales to the entire market.

I testified that this system has worked well – meaning that the economic incentive of additional six month period of exclusive sales of the product has stimulated a significant amount of research and clinical development of pediatric versions of drug products. Since inception of the provision, over 100 drugs have been approved for pediatric indications. In my view, this success is perfectly in line with the Congressional intent of providing the additional six month exclusivity period (i.e., Congress wanted pioneer drug manufactures to develop and bring to market versions of approved drugs suitable for use in pediatric patients, and this has happened with great success).

As is the case for pediatric exclusivity, the patent bonus provisions in Bioshield II seek to provide a *general* economic incentive for companies to develop and bring to market new drugs that can be used as countermeasures. Also as is the case for pediatric drugs, the current market incentives for a company to develop a new countermeasure are insufficient. In my testimony, I observed that there may never be any sales of a product developed as a countermeasure. At a minimum, the market demand for such a drug will be extremely uncertain, both as to whether there will be any significant sales of the product, and certainly as to the profit potential of such a drug. And, as I observed at the hearing, any actual sales of the product may not arise until *after* the test data exclusivity period provided by the Hatch-Waxman act has expired – meaning that this incentive (i.e., market exclusivity for 3 or 5 years after approval) may never yield any commercial benefit for these drugs, because the drugs will not be sold during this limited period after approval.

For the above reasons, I indicated that the creation of a patent bonus provision, such as that outlined in Bioshield II, would, like pediatric exclusivity, create a *general* economic incentive for the private sector to take the risks of investing in, conducting research and development, and bringing new countermeasures to market. Such a market incentive would be clearly understood and definite, and would not be limited to actual sales of the countermeasure, which may be non-existent or on non-commercially viable terms. Thus, I continue to believe the two regimes would be analogous.

The second part of the question asks whether the pediatric extension only applies to a specific, previously approved drug that is evaluated for pediatric approval. The answer is yes. As I tried to explain in the hearing, the pediatric extension solution was a response to the specific problem of an inadequate market incentive for companies to test their products for use in pediatric populations. The market, in simple terms, did not provide an economic incentive sufficient to encourage companies to undertake this difficult task. This is precisely the situation facing companies contemplating development of new countermeasures – an insufficient market incentive to undertake the risky effort of developing a new countermeasure. And, the fact that the pediatric exclusivity bonus is linked to a specific drug does not detract from the analogy. Instead, it addressed the precise problem Congress identified – the encouragement of research and development to support approval of a previously approved drug for use in pediatric patient.

I note that the motivation for this question may be a concern over how the patent bonus is structured in the legislation. I sought in my testimony to indicate that I was addressing the *concept* of a patent bonus provision. It is my belief that creating a defined period of additional patent exclusivity for a drug that is actually being sold is a definite and understandable economic incentive. I would anticipate that the Congress would incorporate into such a provision measures it deemed appropriate to ensure that the measure operates only as intended (e.g., that it would not be possible to obtain multiple extensions of a single product).

The second question posed by Senator Kennedy is:

> It's extremely lucrative for a company to develop a new drug for baldness or obesity or depression. Do you think the incentives in any BioShield II legislation need to be just as high to get big drug companies to participate in biodefense? Will it take billion-dollar subsidies to get them to participate?

In my experience, the vast majority of companies that engage in biomedical research are focused on developing new and effective drugs for treating human diseases that either afflict large numbers of people, or are serious life-threatening illnesses. Contrary to the suggestion in the question, in my experience the primary diseases being investigated are cancer, heart disease, diabetes, Alzheimer's and a variety of communicable diseases. These companies are driven primarily by two factors; namely, the desire to find a solution for a significant unmet medical need, and the ability to deliver a good return on investment. It is an extremely challenging field, and one that provides immense benefits to American public – and indeed the world. Ask any cancer patient that has been given a new hope of being cured.

A significant public and private investment is needed to decipher the mechanisms of disease. But, the true challenge of developing a new drug is to identify how to exploit this scientific knowledge and develop an effective therapeutic intervention. Doing so not only requires innovation as to the design of the drug and intervention, but immense effort to determine how to, for example, manufacture the drug in sufficient quantities and test it to prove that it is safe and effective.

In my experience, those who invest in new drug development are fully aware of these variables. Whether they are early stage venture capital funds or established pharmaceutical or biotechnology companies looking to partner in the drug development process with a small startup company, the questions are the same; namely, (i) is the technology viable, (ii) what is the potential return on investment, and (iii) will the product enjoy an effective period of market exclusivity delivered by patents and test data protection?

Senator Kennedy's question frames the issue as being whether a countermeasure must have the market potential of a "blockbuster" drug. Certainly, a blockbuster pharmaceutical product sold to millions of Americans represents a huge economic incentive. Very few drugs, however, become blockbusters and I believe the premise of the question misplaces the actual focus of the investment decision on a new drug development effort.

In my opinion, the correct question is whether Congress can create a market incentive that makes countermeasure development compete effectively for limited private sector funds and resources. The issue is competition for limited research dollars, not subsidization. In other words, if a company knows that it will have a certain economic reward – an extended patent exclusivity period for a successful drug – then the risk it faces of unsuccessfully developing a new countermeasure, or of developing a drug that will never be sold, can be balanced against a defined market return (i.e., actual sales of a successful product). A definite and understandable market incentive for countermeasures development would make development of such countermeasures attractive to the private sector. Such incentives also would make the investment and development decisions facing a company comparable to those used to decide whether that company should pursue development of drugs for cancer, diabetes, heart disease and other major illnesses affecting the American public.

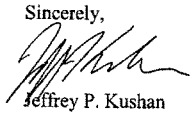
In the question, Senator Kennedy asks whether the market incentives for countermeasures drugs must be comparable to those for what I believe he intended to mean were huge blockbuster drugs. I am unable to put a strict numerical figure on a threshold incentive. Instead, in my view, the degree of potential market return will define the strength of the incentive. Thus, allowing a company to enjoy two additional years of market exclusivity for a drug that earns billions of

dollars of revenue each year will create a very strong incentive, and more countermeasures certainly will be developed in response to that strong incentive. Providing one additional year of exclusivity for any drug will create a smaller, but still discernable incentive. Limiting the patent bonus to drugs that have limited annual sales (e.g., <$100 million annually) will likely make a patent extension incentive ineffective. I note that drugs having only this scale of return are often not funded out of private capital because the risks associated with those drugs is excessive, particularly relative to the limited potential return. For example, one factor a funding entity considers is the scenario of the drug being able to enjoy only new drug exclusivity (i.e., because the drug may not be effectively covered by a patent, or may have its patent invalidated by a generic company after the data exclusivity period for the drug expires). The present environment of assured patent challenges means that most entities must use this "worst case" scenario of a five year period of sales for a new drug product, meaning that the developer of the drug must be able to not only recover the $350 to $750 million of costs of developing and launching the drug, but also deliver a return substantially in excess of those costs. I note that few commercially-focused entities would invest in a drug development venture if the only possibility were to simply recover the investment being made.

As I noted above, I do not believe it is possible to give a simple answer to the question of what the threshold of potential revenue of a countermeasure must be to encourage private entities to undertake developing such drugs, rather than other types of drugs. The best answer I can give is that the market incentive for developing new countermeasures must be strong and dependable enough to offset the negative factors regarding countermeasure development (e.g., limited or no sales of the product). The existing environment which provides only the incentives of assured purchases of countermeasures will induce only a handful of companies to undertake countermeasure development. To encourage companies to prioritize countermeasure development – to pursue development of those, rather than other drug products funded through private capital – requires a market opportunity that is far beyond the opportunities established by Bioshield I.

I hope the answers provided above are useful, and look forward to responding to any further questions the Committees may have.

Sincerely,



Jeffrey P. Kushan

cc: Senator Joseph Lieberman

Alan P. Timmins
President
Chief Operating Officer
AVI BioPharma, Inc.
Hearing on "Bioshield II: Responding to an Ever-Changing Threat"

Answers to questions posed by Senators Kennedy and Schumer:

I am well aware that the wild card patent provision in S. 666 will impose some additional costs on consumers of products with respect to which the bonus is applied. The issue for the Senate is whether this cost is justified as necessary to create a biodefense industry and prepare the country for a Bioterror attack. I firmly believe that the cost to consumers –all consumers – of a Bioterror attack for which we are not prepared certainly exceeds the cost to consumers of the proposed patent bonus. The Congress has already decided that securing pediatric labels on existing products is worth a six month patent extension. So, I believe that it is certainly reasonable for Congress to conclude that providing a two year patent extension as an incentive for the development of a new Bioterror countermeasure is also reasonable. I can simply state that if the Congress does enact this provision it will, in fact, have the desired impact – creating a biodefense industry. The Congress could decide that preparing for a Bioterror attack is not worth the cost to some consumers, but I believe that would be an inappropriate conclusion.

In terms of the specifics of the patent bonus provision, I defer to the Committee's judgment. Mr. Jeff Kushan's testimony outlines some of these specifics in his testimony and I am sure other issues can be raised. One way to ensure that the value of the patent bonus is not disproportionate to the risk and expense incurred by the company developing a bioterror countermeasures is to give the HHS Secretary authority to award "up to 2 years" and to determine how much bonus, if any, is warranted. It's clear that a flat 2 year bonus will not be appropriate in all cases. This will enable the Secretary to ensure that sufficient incentives exist to the Bioterror countermeasures are, in fact, developed and not to unduly burden consumers.

SUBMISSIONS FOR THE RECORD

Aetna Comments: Joint Senate Judiciary and H.E.L.P. Committee Hearing
On S. 666, BioShield II

October 6, 2004
Mark Rubino, RPh., MHA
Chief Pharmacy Officer
Aetna

On behalf of Aetna Inc. , one of the nation's leading providers of health care and pharmacy benefits with 13.4 million medical members, I am pleased to submit for the record our views on how best to prepare this country with respect to bioterrorism threats against America. Aetna supports the goals of both BioShield I and BioShield II (S. 666) as they both seek to promote the availability of drugs and implement other countermeasures against terrorism. However, Aetna is concerned with some aspects of S.666 which, if enacted, could have consequences inconsistent with the overall goals we all support.

As drafted, S. 666 incorporates some provisions which might seriously detract from the bill's overall purpose by needlessly inflating pharmaceutical costs outside the proposed drugs used against terrorism. It could result in increases of pharmaceutical costs for our clients and also have impacts on all pharmaceutical purchasers, including Medicare and Medicaid.

The bill includes an exclusivity feature, under which brand drug manufacturers would be given 2 years of additional patent protection for any drug they choose, no matter how unrelated to addressing bioterrorism and related threats. The brand company merely has to acquire or conduct the research on a countermeasure drug to be eligible to extend the patent of one of its "blockbusters." Conceivably, the research could be of any dollar magnitude, no matter how minimal. This provision could delay the introduction of generic pharmaceuticals and therefore result in increased costs to patients and payers.

The bill doubles the length of the period of market exclusivity from 5 to 10 years for new molecular entities with one identified use as a countermeasure. Countermeasures are defined broadly, so that they may include drugs with widespread uses which are not the intent of the provision. This market exclusivity should be for the counter terrorism indication only.

The bill provides patent extensions for countermeasures for the full period of regulatory review, defined as the time from when the patent is issued to the date of FDA product approval. As drafted, the bill sets no limitations on the number of years of such patent extensions, nor are there any limitations on the number of patent extensions per product. In extreme cases, this provision could be used for drugs that have long been off patent but for which uses as countermeasures have subsequently been identified; in such cases, the bill would reinstate patents for these drugs, forcing generic alternatives off the market.

Aetna supports the extension of Bioshield I, but refinements in the above details will assure a balance between research innovation against terrorism and controlling overall drug expenditures.

Testimony of Carlos Angulo, Partner, Zuckerman Spaeder LLP,
On Behalf of the Coalition for a Competitive Pharmaceutical Market
Before a Joint Hearing of the Senate Health, Education, Labor and Pension Committee
And the Senate Judiciary Committee
October 6, 2004

Good morning Chairman Hatch and Ranking Member Leahy, Chairman Gregg and Ranking Member Kennedy, and distinguished Members of the Committees. My name is Carlos Angulo and I am here to testify on behalf of CCPM, the Coalition for a Competitive Pharmaceutical Market, on S. 666, the Biological, Chemical, and Radiological Weapons Act. I want first to express my appreciation to the Committees for the opportunity to express the Coalition's views on this important bill.

CCPM is an organization of employers, insurers, generic drug manufacturers and others committed to improving consumer access to affordable pharmaceuticals and promoting a vigorous, competitive prescription drug market. CCPM supports public policies that facilitate timely access to affordable pharmaceuticals. The Coalition, of course, also is committed to assisting federal, state, and local governments and the American people in their efforts to develop quick, effective, and accessible responses to bioterrorism.

The Coalition's membership is broad and diverse, and includes numerous prominent purchasers of pharmaceuticals, such as General Motors Corporation, Caterpillar, Inc., Eastman Kodak Company, and Delphi Corporation. On behalf of the Coalition, I would like to share with the Committees today our experience regarding prescription drug cost increases and to underscore our belief that in its current form, S. 666 would dramatically delay generic drugs from coming to market and cause a crippling increase in prescription costs for America's employers, health plans, and consumers.

Impact of Unsustainable Prescription Drug Costs

By way of background, large and small businesses, consumers, unions, governors, the federal government and health plans throughout the nation are aggressively attempting to manage soaring prescription drug costs. These expenditures are growing at annual rates of up to 20 percent and are unsustainable. Current pharmaceutical cost trends are increasing premiums, raising co-payments, pressuring reductions in benefits, and undermining the ability of businesses to compete. CCPM members seeking to continue to provide prescription drug coverage to employees and subscribers face a tremendous challenge in light of these skyrocketing pharmaceutical costs.

For example, General Motors—the largest private provider of health care coverage in the nation, insuring over 1.1 million workers, retirees, and their families—spent over $1.3 billion last year on prescription drugs. Despite GM's use of state of the art management techniques that assure the most appropriate and cost-effective use of prescription drugs, its pharmaceutical bill continues to grow at a rate of 12 percent to 16 percent a year—more than quadrupling the general inflation rate.

Similarly, Eastman Kodak Company, which insures 150,000 covered lives, spends 31 percent of its health care dollars on prescription drugs. Kodak spent roughly $99 million on drugs in 2003 and costs are growing each year.

The experience of insurers is no different. The 41 Blue Cross and Blue Shield Plans that collectively provide health care coverage for 91 million Americans, represented in CCPM by the Blue Cross and Blue Shield Association (BCBSA), are continuing to experience increases in prescription drug costs. The BCBS Federal Employee Program, for example, had drug increases over the last year of 9.67 percent. BCBSA expects these costs to continue to grow, exacerbating the difficulty of providing a meaningful level of coverage for prescription drugs while keeping premiums as affordable as possible.

Such drug cost increases are driven by multiple factors, including higher utilization, direct-to-consumer advertisements, drug price increases, and, especially, delayed generic competition.

If S. 666 passes in its current form, these costs will escalate dramatically and America will have a health care bill it cannot afford to pay.

The Coalition Supports Policies to Strengthen the Nation's Defense Against Bioterrorism

CCPM strongly supports legislation aimed at improving our ability to respond to terrorist uses of chemical or biological weapons. There can be no denying that the events of September 11 forever changed the way in which we live and work. Today, we recognize that in order to protect our employees, our families, and our friends, we must be prepared for every type of situation.

For this reason, we wholly support the goals of the Project BioShield Act of 2004, or "BioShield I," which went into effect just this summer. We also recognize that the effort to prepare our nation against terrorist threats should include incentives to stimulate the development and production of drugs and other countermeasures, and therefore, we support certain provisions of S. 666, such as the provisions for tax credits, fast-track Food and Drug Administration (FDA) review of applications for countermeasures, protection against product liability suits, and the creation of a Terror Weapon Countermeasures Purchase Fund.

CCPM Believes that S. 666 Will Dramatically and Unnecessarily Increase Health Costs

It is also clear, however, that the goal of encouraging a response to bioterrorism must be balanced against the overall costs to American consumers and an already overburdened health care system. Unfortunately, as currently drafted, S. 666 has many unnecessary provisions that will increase costs without significantly benefiting the anti-terrorism effort. Specifically, there are four provisions in the legislation that would seriously hinder employers' ability to provide

affordable health care to their employees; dramatically increase prescription drug costs nationwide, without significant benefit to the anti-terrorism goals of the bill; and in fact, deny public access to affordable versions of the countermeasure products that the bill seeks to make available to the American public

First, S. 666's "wild card" exclusivity provision, found in Section 5(d)(1) of the bill, would give brand pharmaceutical companies a broad mandate to extend a patent for two years on virtually any drug they choose, even if it is completely unrelated to terrorism. This extension of brand company monopolies would force consumers and employers to pay billions of dollars in prescription drug costs beyond what they would pay if generic drugs were permitted to enter the market as provided under current law, without significantly advancing any anti-terrorism goals. Today, drugs that have sales in excess of $2 billion per year are not uncommon. Yet when the patents and other exclusivities on those drugs expire and generic competition begins, the price typically drops between 75% and 90% within a matter of months. Thus, the cost of this provision for a single drug could be in the billions of dollars.

Second, Section 5(f) of S. 666 expands by up to seven years the non-patent statutory exclusivity periods for countermeasures. This change dramatically alters the careful policy balance struck by Congress under the 1984 Hatch-Waxman Act and last year's amendments to that legislation, which sought to provide incentives for innovation while at the same time ensuring swift public access to affordable drug products. S. 666 alters this delicate balance by extending broadly—in certain cases, by over 100%—brand company monopolies at the expense of consumer access to generic drugs.

Third, Section 5(c) of S. 666 would provide patent extensions for the full period taken to complete regulatory review for countermeasures. In certain cases, this provision could go so far as to reinstate patents on drugs that have been off patent, forcing generic alternatives off the market. By denying consumers timely access to more affordable medications—or forcing them off the market altogether—this bill only exacerbates the problems of unsustainable health care costs and the growing number of uninsured Americans.

Fourth, Section 5(f) of S. 666 penalizes the generic industry for merely following the law in submitting generic applications with required patent certifications by providing that a generic company that submits such an application for a generic version of a countermeasure must wait an additional five years for FDA approval beyond what is required under current law. This provision in effect penalizes generic companies for merely attempting to enter the market—contradicting the very intent of the Hatch-Waxman Act.

In short, each of these four provisions of S. 666, standing alone, could cost America's employers, insurers, and consumers billions of dollars, without substantially assisting in the anti-terrorism cause. As innovators, patent-holders and competitors in the world market, CCPM members respect the integrity and value of intellectual property protection. However, we oppose practices that detract from true innovation and new product development and merely serve to preserve old innovations and to expand existing monopolies.

Congress has at one time or another expressly declined to enact into law each of the four provisions discussed above, either during the deliberations leading up to enactment of BioShield I or during passage of other pharmaceutical bills. Lawmakers rightly determined that each of these provisions seriously distorted the balance between encouraging innovation and keeping

health care costs in line. If any one of these provisions were to pass as part of S. 666, it would impose enormous costs on the health care industry. Taken together, the costs imposed by these provisions are unsustainable.

Instead of moving forward with S. 666 as currently drafted, we would encourage the Committees to consider limiting any extension of BioShield I to include provisions such as product liability protections, "fast track" review of countermeasures by the FDA, and incentives in the form of tax credits and public funding. Each of these provisions advances the anti-terrorism goals of the earlier legislation without unduly burdening the health care system.

Conclusion

Every day, the choice of generic products creates substantial savings for consumers; as much as 70 percent to 80 percent when compared to the brand product, resulting in savings of more than $10 billion dollars a year in savings for consumers, employers, insurers, and taxpayers, as well as state and federal governments. Generic drugs play an indispensable role in the search for answers about how to decrease health care costs, while increasing access to important medicines and assuring health care coverage availability. However, S. 666 as currently drafted would dramatically limit Americans' access to affordable drug choices and lead to increased premiums, higher co-payments, fewer health benefits, and reduced access to quality care—particularly for the uninsured and poorly insured.

In these uncertain times, encouraging the development of drugs as countermeasures is a laudable goal. We are looking forward to working with Senate leaders to further enhance BioShield I, while avoiding the adverse effects of S. 666 to healthcare providers, employees, retirees, workers, patients, and the uninsured.

Thank you for allowing me to testify today. I welcome any questions from the Committees.

Statement of the Infectious Diseases Society of America (IDSA) Concerning "BioShield II: Responding to An Ever-Changing Threat" Presented by John G. Bartlett, MD Before the U.S. Senate Committee on Health, Education, Labor, and Pensions and the U.S. Senate Committee on the Judiciary October 6, 2004

Chairman Gregg, Chairman Hatch, Ranking Member Kennedy, Ranking Member Leahy, and Members of the Senate Committee on Health, Education, Labor and Pensions (HELP) and Senate Judiciary Committee, thank you for inviting the Infectious Diseases Society of America (IDSA) to present our views on the critical need for new drugs, vaccines and diagnostics to treat, prevent and detect infectious diseases agents. I am Dr. John Bartlett, chair of the IDSA Task Force on Antimicrobial Availability, Past President of IDSA, and Chief, Division of Infectious Diseases, Johns Hopkins University School of Medicine.

I am testifying today on behalf of IDSA to communicate our strong support for the creation of new legislation that will remove financial disincentives to antiinfective research and development (R&D) so that U.S. physicians will have the tools necessary to take care of very sick patients suffering from infectious diseases. New medicines and diagnostics are critically needed across all areas of infectious diseases medicine.

IDSA represents nearly 7,800 physicians and scientists devoted to patient care, education, research, and community health planning in infectious diseases. The Society's members focus on the epidemiology, diagnosis, treatment, prevention, and investigation of infectious diseases in the U.S. and abroad. Our members include researchers who study infectious microbes, including agents of bioterrorism as well as naturally occurring microbes. Our members also include scientists involved in the development of new pharmaceuticals and vaccines to control, prevent, and treat such infections. Also among our members are the ID clinicians who will be integrally involved should a bioterrorism event or spontaneous natural outbreak occur—an ID specialist discovered the anthrax case that occurred in Florida in 2001. ID clinicians care for patients of all ages with serious infections, including meningitis, pneumonia, tuberculosis, those with cancer or transplants who have life-threatening infections caused by unusual microorganisms, food poisoning, and HIV/AIDS as well as new and emerging infections, such as severe acute respiratory syndrome ("SARS") and West Nile virus. Housed within IDSA is the HIV Medicine Association ("HIVMA"), which represents physicians working on the frontline of the HIV/AIDS pandemic. HIVMA members conduct research, administer prevention programs and provide clinical services to individuals with HIV disease. Together, IDSA and HIVMA are the principal organizations representing infectious diseases and HIV physicians in the United States.

As Senate leaders move forward to develop new legislation, commonly referred to as "BioShield II," IDSA and its members urge you to extend the new legislation's scope beyond pathogens designated as relevant to "bioterror" and apply any new incentives broadly to cover drugs, vaccines and diagnostics needed to treat all areas of infectious diseases, particularly antibiotics to treat antibiotic-resistant organisms. There is an inextricably linked, synergistic relationship between R&D efforts needed to protect against both natural occurring infections and bioterrorism agents. As such, we believe this approach makes perfect sense.

Let me be very clear from the start: IDSA is here today on behalf of patients. We are not here at the request of the pharmaceutical or biotechnology industries nor is our "bad bugs, no drugs" advocacy campaign financed in any way by industry.

Background

On July 21, 2004, the same day that President Bush signed "The Project Bioshield Act" ("Bioshield I"), IDSA issued its landmark report entitled, "*Bad Bugs, No Drugs, As Antibiotic Discovery Stagnates, A Public Health Crisis Brews.*" Copies of that report are available here today. Our report calls attention to a serious public health problem—at the same time that emerging infections and antibiotic resistance are increasing, drug companies are withdrawing from antiinfective R&D. IDSA is particularly concerned about antibiotic R&D, an area in which many pharmaceutical and biotechnology companies have shown the least commitment in recent years, either withdrawing totally or seriously downsizing their dedicated resources and staff. Infectious diseases (ID) and HIV physicians on the frontline of patient care see patients every day who face lengthy hospitalizations, painful courses of treatment and even death because of drug-resistant and other infections. We desperately need new weapons to protect our patients.

Members of Congress are beginning to see the connection between naturally occurring infections and bioterrorism and understand our vulnerability. In their reports on "Bioshield I" in 2003, both the House Government Reform Committee and the Energy and Commerce Committee linked *natural conditions*, including antimicrobial resistance and dangerous viruses, to national security concerns. The Energy and Commerce Report stated "advancing the discovery of new antimicrobial drugs to treat resistant organisms ... may well pay dividends for both national security and public health."

Why Policymakers Should be Concerned

Policymakers have recognized the urgent need to spur R&D related to biodefense, which led to the enactment of "Bioshield I" earlier this year. While the concern about bioterrorism is highly appropriate, it is important to keep things in perspective. Not one American has died from bioterrorism since President Bush first announced "Bioshield I" in February of 2003, but drug-resistant bacterial and other infections have killed tens of thousands of Americans in hospitals and communities across the United States and millions of people across the world during that same short period of time.

Here are some important facts about infectious diseases reported by the World Health Organization and others:

- Infectious diseases are the second leading cause of death in the world and, by far, the leading cause of premature death and disability.
- Worldwide, 15 million deaths annually are caused by infectious diseases.
- Three of the biggest killers—HIV, tuberculosis (TB) and malaria—account for nearly 40 percent of deaths caused by infectious diseases (5.6 million deaths in 2001).
- Diarrheal diseases and respiratory infections are equally as deadly, accounting for 5.8 million deaths in 2001.
- Influenza accounts for 36,000 deaths and more than 200,000 hospitalizations in the United States and 250,000 to 500,000 deaths globally each year. A pandemic influenza outbreak could kill millions in the U.S. alone.
- "Neglected" infectious diseases that primarily affect the poorest populations living in remote areas of the world leave nearly 1 billion people with a lifetime of debilitating illnesses and deformities. These diseases include lymphatic filariasis (5.6 million disability life adjusted years [DALYs—the number of healthy years of life lost due to premature death and disability]), intestinal nematode infections (4.7 million DALYs), leishmaniasis (2.4 million DALYs), schistosomiasis (1.8 million DALYs), sleeping sickness (1.6 million DALYs), onchocerciasis (1.0 million DALYs), dengue (0.7 million DALYs), chagas disease (0.6 million DALYs), and leprosy (0.2 million DALYs). Despite this enormous disease burden, very few public or private resources have been devoted to research on these diseases.
- According to the Global Forum for Health Research, only about 10 percent of health research funding is targeted to diseases that account for 90 percent of the global health burden.

Here are some surprising facts about drug-resistant bacterial infections in the United States:

- Infections caused by resistant bacteria can strike anyone—the young and the old, the healthy and the chronically ill. Antibiotic resistance is a particularly serious problem for patients whose immune systems are compromised, such as people with HIV/AIDS and patients in critical care units.
- About 2 million people acquire bacterial infections in U.S. hospitals each year, and 90,000 die as a result. About 70 percent of those infections are resistant to at least one drug. The trends toward increasing numbers of infection and increasing drug resistance show no sign of abating.
- Resistant pathogens lead to higher health care costs because they often require more expensive drugs and extended hospital stays. The total cost to U.S. society is nearly $5 billion annually.
- The pipeline of new antibiotics is drying up. Major pharmaceutical companies are losing interest in the antibiotics market because these drugs simply are not as profitable as drugs that treat chronic (long-term) conditions and lifestyle issues.

- Resistant bacterial infections are not only a public health problem; they have national and global security implications as well.
- The Institute of Medicine and federal officials have identified antibiotic resistance and the dearth of antibiotic R&D as increasing threats to U.S. public health.

Emerging and Re-emerging Infectious Diseases

Market forces alone will not solve the current crisis in infectious diseases drug, vaccine and diagnostic R&D—that's why we need innovative public policy changes such as those that the Senate HELP and Judiciary Committees are now contemplating.

Robust R&D programs are needed to respond successfully to existing infectious diseases as well as new threats on the horizon. More than three-dozen new infectious diseases have been identified since the 1970s that have impacted the United States and more vulnerable countries. The list includes HIV/AIDS, severe acute respiratory syndrome (SARS), West Nile virus, Lyme disease, hepatitis C, a new form of cholera, waterborne disease due to *Cryptosporidium*, foodborne disease caused by *E. coli* 0157:H7, and a plethora of neglected diseases that primarily affect patients in the developing world.

Some of these diseases have no treatment except for supportive care. For diseases that do have effective treatments, complacency can stifle new research and allow us to be caught off guard when current treatments become less effective due to resistance. This has been the case with tuberculosis (TB). It has been 30 years since a new class of antibiotic was approved to treat TB despite the fact that it is the second most common microbial cause of death in the world. Doctors also are concerned about the rapid rate at which other bacterial infections, such as gonorrhea and syphilis, are becoming resistant to drugs. Finally, for diseases such as TB, AIDS, and malaria, which have notoriously complex and sometimes toxic treatment regimens, there is a substantial need for new drugs that are not only more effective but easier to deliver to the patient so that greater drug adherence and, ultimately, successful care and treatment will be achieved.

Antibiotic-Resistant Bacterial Pathogens: Why IDSA is Concerned

New treatments, preventions, and diagnostics are clearly needed in all areas of infectious diseases medicine. However, IDSA is particularly concerned that the pharmaceutical pipeline for new antibiotics is drying up. Infectious diseases physicians are alarmed by the prospect that effective antibiotics may not be available to treat seriously ill patients in the near future. There simply aren't enough new drugs in the pharmaceutical pipeline to keep pace with drug-resistant bacterial infections, so-called "superbugs." Antibiotics, like other antimicrobial drugs, have saved millions of lives and eased patients' suffering. The withdrawal of companies from antibiotic R&D is a frightening twist to the antibiotic resistance problem and, we believe, one that has not received adequate attention from federal policymakers.

Until recently, company R&D efforts have provided new drugs in time to treat bacteria that became resistant to older antibiotics. That is no longer the case.

A recent analysis published in the journal *Clinical Infectious Diseases* found only five new antibiotics in the R&D pipeline out of more than 506 drugs in development. The authors evaluated the websites or 2002 annual reports of 15 major pharmaceutical companies with a track record in antibiotic development and seven major biotechnology companies. Their analysis revealed four new antibiotics being developed by pharmaceutical companies, and only one antibiotic being developed by a biotech company. By comparison, the analysis found that the pharmaceutical companies were developing 67 new drugs for cancer, 33 for inflammation/pain, 34 for metabolic/endocrine disorders, and 32 for pulmonary disease. The biotech companies were developing 24 drugs for inflammation/immunomodulators, 14 drugs for metabolic/endocrine disorders, and 13 for cancer.

The end result of the decline in antibiotic discovery research is that the Food and Drug Administration (FDA) is approving few new antibiotics. Since 1998, only 10 new antibiotics have been approved, two of which are truly novel—i.e., defined as having a new target of action, with no cross-resistance with other antibiotics. In 2002, among 89 new medicines emerging on the market, none was an antibiotic.

The Institute of Medicine's (IOM) 2003 report on microbial threats reinforces the point, noting that although at first glance the situation with respect to antibiotics currently in clinical development looks encouraging, not one *new class* of antibiotics is in late-stage development. "Rather these 'new' antibiotics belong to existing classes, including macrolides and quinolones, that have been used to treat humans for years," IOM said.

Unfortunately, both the public and private sectors appear to have been lulled into a false sense of security based on past successes. The potential crisis at hand is the result of a marked decrease in industry R&D, government inaction, and the increasing prevalence of resistant bacteria.

IDSA has investigated the decline in new antibiotic R&D for more than a year, interviewing stakeholders from all sectors. We have met with officials from FDA, the National Institute of Allergy and Infectious Diseases (NIAID), the Centers for Disease Control and Prevention (CDC), congressional members and staff, executives from leading pharmaceutical and biotechnology companies, representatives from public-private partnerships that are focused on infectious diseases-related product development, patients, and other stakeholders. Based on our investigation, IDSA is convinced that the pharmaceutical and biotechnology industries are clearly best situated to take the lead in developing new antibiotics needed to treat bacterial diseases. They are the only player with a track record of success. Consequently, industry action must become the central focus of an innovative federal public health effort designed to stimulate antibiotic R&D.

Why Naturally Occurring Infections Should Be Included Within "Bioshield II" & "Bioshield I"

IDSA strongly supports including all infectious diseases, and particularly antibiotics used to treat antibiotic-resistant organisms, within the scope of "Bioshield II." Research related to both naturally occurring infections and bioterrorism agents seeks to understand

how these organisms cause disease, the immune system response to these pathogens, the development of drug resistance, and how antibiodies and medicines protect against them. As such, infectious diseases and bioterrorism countermeasure R&D are inextricably linked. In the end, we need antibiotics, anti-virals, and other drugs that can be utilized against a variety of diseases, and vaccines that can be adapted to a variety of organisms. Extending the scope of "Bioshield II" to include infectious diseases that are naturally occurring will enhance the research needed to develop bioterrorism countermeasures and vice versa.

We also urge that the "guaranteed market" provisions of "Bioshield I" be expanded to be applied to the development of all antibiotics, not just those intended to fight bioterror agents of present concern. Antibiotic resistant organisms that currently threaten Americans in hospitals and communities can have future national and global security implications as well. Virtually all of the antibiotic-resistant pathogens that exist naturally today can be bio-engineered through forced mutation or cloning. In addition, genetic manipulation of existing pathogens could render them resistant to currently available antibiotics. A better understanding of the mechanisms related to drug resistance and tools that could be derived from such research may help U.S. public health officials as they monitor and respond to any future bioterrorism episodes that involve genetically engineered resistant pathogens. Thus, expanding the procurement provisions found in "Bioshield I" to antibiotics used to treat natural occurring bacterial infections will spur the development of new antibiotics that would provide benefits against naturally occuring infections and bioterrorism.

While "BioShield I" loosely could be applied to the development of antibiotics used to treat naturally occurring resistant organisms, it is not likely that such antibiotics will be listed as a priority of the Administration under "BioShield I." "BioShield I"-related funding mostly or entirely will be utilized for procurement of bioterrorism countermeasures where the government is the sole market. There is a substantial civilian market for antibiotics, with the government only a marginal player. In those cases, it won't be the government that is the principal purchaser. However, the government could contribute to and administer a pool of funds from federal and charitable sources that will make up the guarantee pool. Then it can add the tax, intellectual property, and other incentives from "Bioshield II" to make it all work. This approach would be consistent with our needs for bioterrorism preparedness and provide a much-needed benefit to our public health infrastructure.

Pharmaceutical Charity Helps, But Is Not the Solution

Some policymakers and members of the public place the onus on the pharmaceutical industry, saying that companies should act responsibly and ensure that new drugs and vaccines are available as needed. The pharmaceutical industry supports many good works *pro bono*. Some examples include Merck & Co.'s efforts related to River Blindness; efforts by Bristol-Myers Squibb, Pfizer, and other drug companies related to global AIDS; and GlaxoSmithKline's malaria and AstraZeneca's TB drug discovery initiatives. Nevertheless, companies are responsible to their shareholders and cannot alter their fundamental business strategies in ways that would place their bottom lines at risk.

Drug and vaccine R&D is expensive, risky, and time-consuming. As such, companies are most likely to invest in products for which a strong return on investment is likely, such as drugs that treat long-term, chronic illnesses, lifestyle issues, and products that benefit people in developed countries who can afford to pay for them. Most antiinfectives, particularly antibiotics, which are used for short durations (7-14 days), face restricted use to avoid the development of resistance, resistance limits effectiveness and profitability, etc.; vaccines; and medicines desperately needed in the developing world are being left out.

Policymakers and the public should have no illusions that future pharmaceutical charity will be sufficient to address the existing and emerging infectious pathogens that threaten U.S. and global health. Instead, IDSA believes the onus is on the federal government to lure industry to antiinfective R&D as a means to protect U.S. public health and strengthen national security.

Potential Solutions

IDSA's report, "*Bad Bugs, No Drugs, As Antibiotic Discovery Stagnates, A Public Health Crisis Brews,*" offers a number of solutions for policymakers to consider, and builds upon several solutions included in the "Biological, Chemical, and Radiological Weapons Countermeasures Research Act" (S. 666), introduced by Senators Lieberman and Hatch in 2003. IDSA's investigation of the "bad, bugs, no drugs" problem has revealed that the solutions most likely to spur R&D within major pharmaceutical companies include those that provide financial benefits prior to a drug's approval (e.g., tax credits for R&D), commence at the time of approval (e.g., wild-card patent extension), reduce the costs of clinical trials (e.g., FDA flexibility concerning the evidence necessary to demonstrate safety and efficacy; NIAID-sponsored research to develop rapid diagnostics tests, screen candidates, etc.), and reduce companies' risks (e.g., liability protections). R&D at smaller biotechnology companies also could be stimulated through statutory and administrative changes. Specific recommendations for FDA and NIAID action may be found in IDSA's report.

Following is a list of potential legislative solutions that may help to spur R&D of drugs, vaccines, and diagnostics to treat, prevent, and detect bacteria, viruses, parasites, fungi and other infectious organisms. IDSA does not claim to possess all of the answers, but we believe a combination of the legislative solutions listed below will help. Critical priority incentives that we believe will have the greatest impact are indicated. Policymakers should use these recommendations to shape a framework for governmental action.

Commission to Prioritize Antimicrobial Discovery [CRITICAL PRIORITY]
Establish and empower an independent Commission to Prioritize Antimicrobial Discovery to decide which infectious pathogens to target using the legislative R&D incentives listed below.

Supplemental intellectual property protections:

- "Wild-card patent extension." [CRITICAL PRIORITY]

A company that develops and receives approval for a priority antiinfective could extend the market exclusivity period of another FDA-approved drug as long as the company commits to invest a portion of the profits derived during the extension period back into antiinfective R&D.

- Restoration of all patent time lost during FDA's review of and clinical trials undertaken related to priority antibiotics and antiinfectives
- Extended market and data exclusivity similar to what has been successfully implemented for pediatric and orphan drugs

Other potential statutory incentives:

- Tax incentives for R&D of priority antiinfectives [CRITICAL PRIORITY]
- Measured liability protections [CRITICAL PRIORITY]
- Additional statutory flexibility at FDA regarding approval of antibiotics and other antiinfectives, as needed
- Antitrust exemptions for certain company communications
- A guaranteed market similar to that provided in Bioshield I for priority antibiotics that target resistant bacterial and other antiinfectives, as appropriate

Establish similar statutory incentives to spur R&D for rapid diagnostic tests for targeted pathogens, which will help to reduce the cost of clinical trials

Potential statutory incentives of interest to small biopharmaceutical companies:

- Waive FDA supplemental application user fees for priority antibiotics and other antiinfectives
- Tax credits specifically targeting this segment of the industry
- Small business grants

Support synergistic partnerships that focus on infectious diseases medicines:
A growing number of international public-private partnerships are focusing on the discovery of medicines to treat infectious diseases in the United States and globally. Initiatives like the International AIDS Vaccine Initiative, the Medicines for Malaria Venture, and the Global Alliance for TB Drug Development offer promising opportunities to advance product R&D in areas that have languished in the past. Public-private partnerships have adopted business models that exploit the venture capital approach to investment in new product R&D. Such initiatives receive the bulk of funding from the public and philanthropic sectors. They involve for-profit partners by seeking in-kind contributions from industry. The commitment of U.S. public dollars for these and similar initiatives would take advantage of the entrepreneurial spirit possessed by many researchers and humanitarians.

In addition to funding public-private partnerships, policymakers should seriously consider ways to prompt companies to inventory their shelves for promising drug candidates that could be donated to the partnerships for development. Such candidates exist, and companies recently have shown some interest in donating them. This is not a current priority for companies, however, because the resources required would have to be diverted from other efforts.

Conclusion

The time for talk has passed—it's now time to act. The "bad bugs, no drugs" problem is growing more severe, and patients are suffering. Even if all of the incentives outlined in our testimony were implemented today, it likely would take 10 or more years for companies to move safe and effective new drugs, vaccines and diagnostics to market. The federal government must take decisive action now to address the burgeoning problem of infectious diseases, particularly the lack of antibiotics to treat resistant organisms.

Government-sponsored research and refinement of existing regulations, policies, and guidance can help to address the overall problem, fill in some of the gaps in drug, vaccine, and diagnostics development, and help to reduce the cost of discovery and development. Industry action, however, must remain policymakers' central focus. Policymakers must remove financial disincentives to antiinfective R&D as a means to stimulate pharmaceutical and biotechnology companies to invest in the discovery of tools to treat, prevent, and detect infectious diseases.

Specific to antibiotics, the past two decades of antibiotic development clearly have demonstrated that we no longer can rely on existing market forces to keep companies engaged in this area of drug discovery and development. Should additional companies' antibiotic R&D infrastructures be dismantled, it will take years to establish new programs—or this expertise could simply be lost forever. New antibiotics are desperately needed to treat serious as well as common infections. The bacteria that cause these infections are becoming increasingly resistant to the antibiotics that for years have been considered standard of care, and the list of resistant pathogens keeps growing. It is not possible to predict when an epidemic of drug-resistant bacteria will occur—but we do know it will happen.

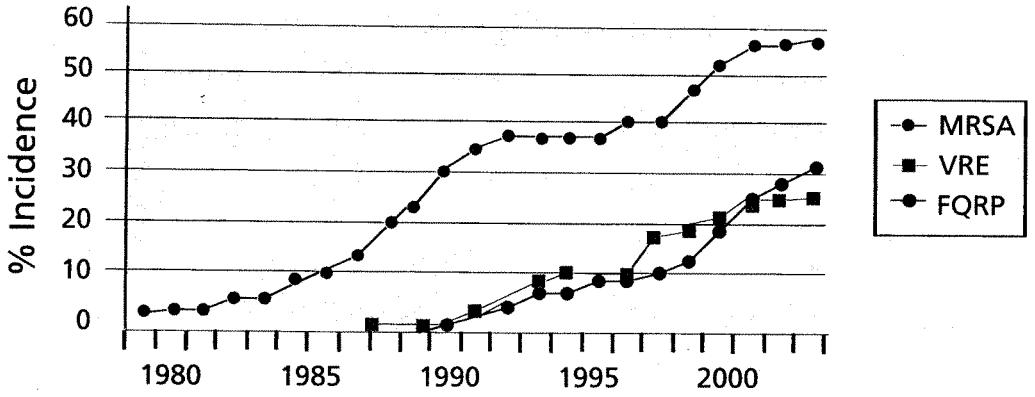
Drugs, vaccines and diagnostics also are needed across the spectrum of infectious diseases medicine. Conquering AIDS, TB, malaria, the neglected diseases found primarily in developing countries, and the next emerging infection will require renewed vision, creative policymaking and righteous action.

"Bioshield II" provides a critical opportunity to spur the development of new tools to protect Americans and the global community against the scourge of infectious diseases, particularly antibiotic resistant organisms, and bioterrorism. We urge congressional leaders to show bold leadership in creating this legislation and urge its quick passage.

We appreciate the opportunity to testify before the Senate Health, Education, Labor and Pensions Committee and Senate Judiciary Committee. We look forward to working with you in the coming months to develop federal legislation to spur the tools infectious diseases and HIV/AIDS physicians need to treat our seriously ill patients.

Thank you.

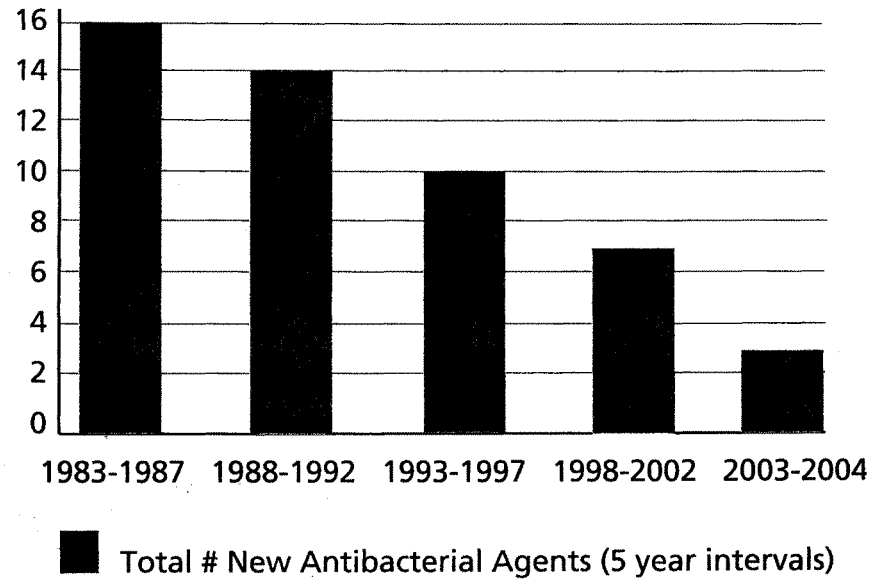
Chart 1: Resistant Strains Spread Rapidly



Source: Centers for Disease Control and Prevention

This chart shows the increase in rates of resistance for three bacteria that are of concern to public health officials: methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant enterococci (VRE), and fluoroquinolone-resistant *Pseudomonas aeruginosa* (FQRP). These data were collected from hospital intensive care units that participate in the National Nosocomial Infections Surveillance System, a component of the CDC.

Chart 2: Antibacterial Agents Approved, 1983-2004



Source: Spellberg et al., *Clinical Infectious Diseases*, May 1, 2004 (modified)

IDSA

PRESS RELEASE
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IDSA Calls for Federal Legislation to Protect Patients Against Infectious Diseases, Spur Anti-infective Development

Infectious Disease Physicians Urge Senators to Cosponsor "Bioshield II"

Congress should act soon to introduce and enact legislation to spur the development of new medicines and diagnostics to treat infectious diseases, particularly new antibiotics that target drug-resistant infections. That was the key message of the Infectious Diseases Society of America (IDSA) in testimony presented today before a unique joint hearing of the U.S. Senate Committee on Health, Education, Labor, and Pensions (HELP) and the Senate Judiciary Committee.

Leaders from both Senate committees are working together to develop novel federal legislation commonly called "Bioshield II" intended to spur the development of treatments, preventatives, and diagnostics related to bioterrorism preparedness and response. The new legislation would build on "The Project Bioshield Act" ("Bioshield I"), which was signed into law July 21, 2004, the same day that IDSA issued a major report, *Bad Bugs, No Drugs: As Antibiotic Discover Stagnates ... A Public Health Crisis Brews.*

Through today's testimony, IDSA hopes to convince Senate leaders to extend the scope of Bioshield II beyond bioterrorism to remove financial disincentives in all areas of infectious diseases research and development, particularly for antibiotics to treat drug-resistant infections. "There is an inextricably linked, synergistic relationship between research and development efforts needed to protect against both naturally occurring infections and bioterrorism agents," said John G. Bartlett, MD, chief of the division of infectious diseases at the Johns Hopkins University School of Medicine and chair of IDSA's Task Force on Antimicrobial Availability. "As such, we believe this approach makes perfect sense."

Research related to both naturally occurring infections and bioterrorism agents seeks to understand how these organisms cause disease, the immune system response to these pathogens, the development of drug resistance, and how antibodies and medicines protect against them. "Extending the scope of 'Bioshield II' to include infectious diseases that are naturally occurring will enhance the research needed to develop bioterrorism countermeasures and vice versa," Dr. Bartlett said.

Worldwide, 15 million deaths are caused by infectious diseases each year, making infectious diseases the second leading cause of death and the leading cause of premature death and disability. ID physicians are seriously concerned about the need for new drugs, vaccines, and diagnostics to protect their patients against naturally occurring infections, including HIV/AIDS, tuberculosis, malaria, severe acute respiratory syndrome (SARS), and pandemic influenza.

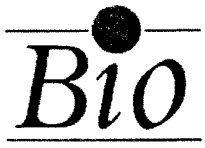
Infectious diseases physicians also have become increasingly alarmed about the rise in drug-resistant bacterial infections and the simultaneous decline in the development of new antibiotics. About 2 million people acquire bacterial infections, such as methicillin-resistant *Staphylococcus aureus (MRSA)*, in U.S. hospitals each year, and 90,000 die as a result. About 70 percent of those infections are resistant to at least one drug. Surprisingly, a recent analysis found only five new antibiotics in the R&D pipeline out of more than 506 drugs in development. Since 1998, only 10 new antibiotics have been approved, and only two of those are truly novel—i.e., defined as having a new target of action, with no cross-resistance with other antibiotics. In 2002, among 89 new medicines emerging on the market, none was an antibiotic. This problem is further highlighted in IDSA's *Bad Bugs, No Drugs* report.

Infectious diseases and HIV physicians on the frontline of patient care see patients every day who face lengthy hospitalizations, painful courses of treatment and death because of drug-resistant and other emerging and reemerging infections. "We desperately need new weapons to protect our patients. Major pharmaceutical companies are losing interest in the anti-infectives market because most infectious diseases drugs simply are not as profitable as drugs in many other areas of medicine, including those used to treat chronic, long-term conditions and lifestyle issues," Dr. Bartlett said.

"Market forces alone will not solve the brewing crisis in infectious diseases medicine—that's why we need innovative public policy initiatives such as those that the Senate HELP and Judiciary committees are now contemplating," said Dr. Bartlett.

IDSA's testimony and the full *Bad Bugs, No Drugs* report are available on the Society's website at www.idsociety.org/badbugsnodrugs.

IDSA is an organization of physicians, scientists and other health care professionals dedicated to promoting human health through excellence in infectious diseases research, education, prevention, and patient care. The Society, which has nearly 7,800 members, was founded in 1963 and is headquartered in Alexandria, Va. For more information, visit www.idsociety.org.



BIOTECHNOLOGY
INDUSTRY
ORGANIZATION

STATEMENT OF THE
BIOTECHNOLOGY INDUSTRY ORGANIZATION

FOR THE SENATE COMMITTEE ON
HEALTH, EDUCATION, LABOR, AND PENSIONS
AND THE SENATE COMMITTEE ON THE JUDICIARY

HEARING ON PROJECT BIOSHIELD II

OCTOBER 6, 2004

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This statement is submitted by the Biotechnology Industry Organization (BIO), an organization representing over 1,000 companies, universities, research institutions, state biotechnology associations and affiliates in all 50 states.

BIO actively supported the passage of S. 15, The Project BioShield Act of 2004, earlier this Congress. The Act was a critical first step for developing a viable biodefense industry in the United States.

A significant obstacle to implementing The Project BioShield Act of 2004 is that participating private sector companies face extraordinary risks due to the potential for product liability litigation. BIO applauds the Committee's commitment to examine the liability issues and urges the Committee to address them in BioShield II. Additionally, BIO urges the Committee to ensure that The Project BioShield Act is in fact promptly and fully implemented, beginning with the determination of material threats and commitments to purchase countermeasures to address those threats.

As we indicated in prior Congressional testimony, companies engaged in developing and manufacturing biomedical countermeasures face unique risks because of the very nature of the underlying threat. Specifically, the threat ranges from natural pathogens delivered intentionally by surprising means to microorganisms genetically engineered for nefarious purposes. For some potentially important countermeasures it may be difficult to distinguish the drug side effect profile from the bio-threat pathology.

Additionally, because of the deadly nature of bio-weapons, human efficacy data cannot ordinarily be obtained in advance of an attack. Thus, preclinical and clinical testing data for biomedical countermeasures will necessarily be less complete than for drugs and vaccines targeting other diseases. Moreover, unlike most pharmaceuticals which are administered to very targeted groups, biological countermeasures are likely to be administered to the population at large. Because of the wider distribution, there will be a greater incidence of contemporaneous effects that will invariably be associated – correctly or incorrectly – as a side effect of the countermeasure.

Further, the administration of most if not all biological countermeasures will likely involve a far greater government role than for other drugs and vaccines. Thus, a private manufacturer that can normally initiate important changes in labeling or product recalls if it believes necessary, may not have the ability to mitigate the prospect for becoming embroiled in massive litigation.

The Department of Defense's anthrax vaccine inoculation effort, begun in the 1990's is a case in point. The controversial initiative has already attracted significant litigation against both the Department and BioPort, the manufacturer of the vaccine. Importantly, the manufacturer of that vaccine has been protected with an indemnification under P.L. 85-804. Under P.L. 85-804, agencies may indemnify entities involved in "unusually hazardous risks" when it is in the interest of national security to do so. The covered entity shares the risk of liability by agreeing to provide specified levels of insurance and the federal government's exposure is limited to claims not covered by the required insurance. The authority of P.L. 85-

804 has been used sparingly since it was first established fifty years ago, but it has enabled companies to carry out hazardous projects for the government, ranging from nuclear research to chemical weapons destruction and the like.

For companies that manufacturer one or a small number of countermeasures, P.L. 85-804 can help mitigate some of the extraordinary risks that they face. However, for companies that have multiple products, even P.L. 85-804 leaves the door open for ruinous litigation because the indemnification is only triggered after company-wide insurance coverage has been exhausted. This leaves companies potentially exposed in the event that other routine claims not covered by the indemnification are filed in the same insurance policy period.

Moreover, future manufacturers of anthrax vaccine and other countermeasures will likely not even be able to take advantage of the limited protection of P.L. 85-804. The President has specifically instructed agencies *not* to utilize the indemnification authority under P.L. 85-804 when the Support Anti-terrorism by Fostering Effective Technologies (Safety) Act of 2002, P.L. 107-296, Subtitle G, is available. In Executive Order 13286, (February 28, 2003), the President made clear his preference for use of the Safety Act and, by requiring additional determinations and approvals, made it more difficult for agencies to offer indemnifications under P.L. 85-804 in the context of homeland security initiatives.

However, the Safety Act was enacted as part of the Homeland Security Act in 2002, and is focused on technologies developed *to combat or prevent terrorist acts*. It does not effectively protect the biotechnology industry against risks associated with the development and manufacture of biomedical countermeasures. The Safety Act limits liability only when the liability arises from an act of terrorism. Specifically, the Safety Act applies to "claims arising out of, relating to, or resulting from an act of terrorism when qualified anti-terrorism technologies have been deployed in defense against or response or recovery from" an act of terrorism.

In the absence of a specific terrorist act, such a liability limitation approach is completely ineffectual for biological countermeasures inasmuch as the primary dangers are injuries associated with side effects and the inability to fully test and control the use of the countermeasures, as explained above. Thus, the Safety Act would leave vaccine and other countermeasure producers exposed except in the narrow instance of a specific terrorist act. Additionally, the Safety Act includes a mandatory insurance requirement which. For drugs that have not received approval by the Food and Drug Administrations but which may be distributed for emergency use under the BioShield Act, it will be virtually impossible to obtain insurance. Moreover, Safety Act coverage is determined by the Department of Homeland Security on a product-by-product basis and companies have been faced with a lengthy and cumbersome qualification process that requires companies to demonstrate prior use and effectiveness. Given the experimental nature of many biological countermeasures, they are often unproven until there is an act of terrorism.

In the context of the smallpox threat, Congress has appropriately recognized and addressed the unique risks and extended the coverage of the Federal Tort Claims Act to private sector entities that manufacture, distribute, or administer small pox vaccine. 42 U.S.C. 233(p).

Thus, the private manufacturers of the vaccine are covered under an indemnification under P.L. 85-804 and would have the same protection from liability that federal employees have under the Federal Tort Claims Act. The Department of Health and Human Services has characterized the need for liability protections for manufacturers and distributors of small pox countermeasures as "integral to ensuring maximum participation in the vaccination program." Notice, 58 Federal Register 4212 (January 28, 2003).

BIO believes that a similar approach should be used for all countermeasures designated under the Project BioShield Act of 2004. Of course, BIO does not seek to shield a company from liability for actions caused by fraud or gross misconduct. We urge the Committee to amend section 224 of the Public Health Service Act to cover these other countermeasures, just as the smallpox vaccine is currently covered.

Additionally, BIO urges the Committee to encourage the Administration to implement Project BioShield swiftly. To date, the Department of Homeland Security has not issued any determinations of material threats nor has it taken any steps to conduct a call for countermeasures to address bioterrorism threats, as contemplated in the Project BioShield Act. In the absence of a specific signal and commitment to purchase, companies are reluctant to invest the necessary resources to develop biological countermeasures.

BIO stands ready to assist the Committee in ensuring that BioShield becomes an effective program in the Administration's war on terror. We thank you for your time and attention to this matter.

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TESTIFYING BEFORE THE UNITED STATES SENATE

COMMITTEE ON HEALTH, EDUCATION, LABOR, AND PENSIONS

AND

COMMITTEE ON THE JUDICIARY

REGARDING THE

BIOSHIELD II: RESPONDING TO AN EVER-CHANGING THREAT

October 6, 2004

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Chairman Gregg, Chairman Hatch, Senator Kennedy, Senator Leahy, and Members of the Committees, it is an honor for me to testify before you today regarding liability and antitrust issues surrounding the creation of an effective bio-defense industry in the United States. I would like to recognize the commitment and leadership on the issue of bio-defense displayed by each of you in the drafting and passage of the Project Bioshield Act of 2004. Specifically, the foresight of Chairman Hatch and Senator Lieberman in introducing similar legislation soon after the attacks of 2001 and the leadership of Chairman Gregg and Senator Kennedy in introducing S. 15 and seeing it through to passage are to be commended. America is safer thanks to your leadership and actions.

My testimony today is based on direct experience advising government contractors, pharmaceutical, and bio-tech companies throughout America and throughout the world on how to bring the best possible homeland security and anti-terrorism solutions to both the government and private markets. My work over the last three years has centered on addressing liability issues surrounding anti-terror goods and services, including, specifically, bio-defense countermeasures. My firm and I played a key role in the drafting and passage of the SAFETY Act, including representing all four entities that received the first certifications under the Act on June 18, 2004. There is no greater concern – particularly, for public corporations in the post- Sarbanes/Oxley environment – than ensuring a balance between responding to the nation's need for high-quality anti-terror technology and protecting corporate assets from unnecessary, expensive litigation that threatens

the very existence of these companies and prevents effective countermeasures from being deployed.

In the area of bio-defense, we have worked closely with a number of pharmaceutical and bio-tech companies to ensure that the Project Bioshield Act of 2004 addressed what they perceived as obstacles to entering the bio-defense market. I am happy to testify that through the leadership of the Bush Administration and Congress, this landmark legislation has achieved a great deal. It provides the Federal government the ability to ensure industry a market for bio-defense products. It streamlines the contracting process to attract great interest from non-traditional government contractors. It provides funding to allow the Federal government to purchase and stockpile critical countermeasures. And it allows the President to act during an emergency to get the best countermeasures available into the hands of our public health officials, regardless of whether every regulatory step required in peacetime has been completed. In short, Project Bioshield is a positive step in protecting the nation.

Congress now has the opportunity to build upon this success by enacting Bioshield II. There are two issues that I would like to discuss today that merit consideration as part of Bioshield II. First, Congress should act to remove obstacles caused by liability concerns that prevent bio-defense countermeasures from coming to market. Second, Congress should encourage the use of existing antitrust authorities to stimulate and streamline industry participation in this critical market.

Liability Must be Addresses to Have a Successful Bio-Defense Industry

Make no mistake – liability concerns are preventing critical bio-defense measures from being developed and coming to market. There is a clear difference between the liability concerns of a company engaged in day to day drug development and sales and the concerns of a bio-defense provider. First and foremost, these countermeasures are, by their very nature, meant to prevent or mitigate the impact of a criminal, terrorist act. Such acts are unpredictable and the means to address their impact must rely only upon available intelligence, predictive models, and, to a large degree, luck. This is not an environment that any responsible company can enter lightly. And without an effort to address the issue of liability, it is a market I regret to say many of the best and brightest will simply avoid.

Nature of the Liability Threat

Manufacturers of countermeasures produced under Project Bioshield risk exposure to devastating product liability lawsuits to a far greater degree than typical drug companies. Project Bioshield specifically contemplates that such countermeasures may be made available without the usual battery of clinical trials required for other FDA-approved products. Safety and efficacy data must be derived, for the most part, from animal trials since healthy humans cannot be exposed toxic agents during testing for obvious reasons. Thus, these critical

countermeasures must be developed and are likely be deployed without the full battery of testing typical of other drugs.

Moreover, the distribution and administration of countermeasures in response to a bioterrorist attack will most certainly require the government's enhanced role in recommending, distributing and administering countermeasures during a crisis. The very nature of deploying countermeasures in the fog of a crisis will clearly expose manufacturers to unknown and unquantifiable liability that cannot be addressed simply by good laboratory and manufacturing practices and insurance.

Additionally, the government may rightly decide to purchase and stockpile countermeasures with undetermined side effects until a better countermeasure is developed. These stockpiles could remain in place for years, only to be deployed in an emergency. Further, the government has the ability now to administer countermeasures developed under Bioshield, even without full regulatory approval.

Finally, the market for bio-defense countermeasures is limited primarily to government stockpiles. Thus, unlike with drugs produced to treat illness or even infectious disease, there is no predictable, reoccurring market that would allow a company to spread the liability risk across a large volume of drugs for a period of years.

Even as the government has begun to purchase Bioshield countermeasures, it has no current way to resolve issues of liability - an issue of grave concern to

industry - with any degree of certainty as part of the procurement process. The net impact of this atmosphere results in needed countermeasures not being developed and deployed, thereby exposing the economy, and the nation as a whole, to far greater potential liability due to the lack of available effective countermeasures in the event of attack. Either way, the Federal government is likely to the bear both the human and financial cost of such an attack as it did on September 11th. But by failing to account for these costs before an attack, countermeasures will not be developed and the nation will be more exposed to attack.

Available Liability Mitigation Tools are Inadequate

Congress should act to address liability in, at a minimum, three ways: by encouraging expanded use of existing indemnification authorities; by expanding the SAFETY Act to cover vaccines and other countermeasures deployed prior to a terrorist attack; and, by expanding the compensation scheme provided for smallpox countermeasures to cover all countermeasures produced under Project Bioshield.

Currently, there exists only two ways the Federal government can mitigate the liability concerns for providers of countermeasures other than smallpox vaccine - through Federal indemnification under Public Law 85-804 and through designation/certification under the SAFETY Act.

Public Law 85-804

As you are aware, Public Law (P.L.) 85-804 (August 28, 1958, codified at 50 U.S.C. § § 1431 - 1435) grants the President extremely broad authority that allows a Federal government contractor to obtain financial or other forms of relief under certain circumstances, even when the government may have no express legal obligation to grant such relief, or when there are express prohibitions against such relief contained in other statutes, regulations, or common law. Under this authority, the heads of designated departments or agencies have the discretionary power to provide contractors with government indemnity when they are engaged in unusually hazardous or nuclear activities and when it is in the interest of the national defense to provide such indemnity. Of course, the liability protections offered by P.L. 85-804 still requires years of litigation until victims are ultimately compensated.

In essence, indemnification under P.L. 85-804 relies upon the usual tort system and simply places the Federal government in the position of an insurer where payments are made only after all claims have been adjudicated in the court system and judgments have bee rendered. This rather lengthy process does not result in compensation to victims being paid in a timely manor nor does it place any effective limits on the Federal government's contingent liabilities when it acts in this capacity. However, given the types of risk it is meant to address, P.L. 85-804 has proven to be an effective means of addressing liability concerns for the deployment of unusually hazardous technologies to the Federal government.

This authority has been invoked by the Department of Health and Human Services (which was first granted the authority in October 2001 following the anthrax attacks) in agreements involving the donation of smallpox vaccine by Wyeth and Aventis Pasteur to the Federal government in 2001. However, HHS will not, as a matter of HHS policy, address the issue of indemnification prior to award of a contract for a countermeasure. This policy leaves potential providers of bio-defense countermeasures in the position of having to expend scarce resources to prepare and submit a proposal that may result in a contract that cannot be accepted due to the lack of liability protections should HHS ultimately refuse to provide indemnification. More often, companies simply refuse to bid at all due to the lack of certainty on the issue of liability. This has resulted in the largest, and far more experienced, drug companies with the necessary expertise to address this threat being left on the sidelines of the war on terror - a result that does not serve the nation well.

In addition, on February 28, 2003, President Bush significantly modified E.O. 10789 implementing P.L 85-804 by adding additional requirements for heads of agencies and departments considering requests from contractors seeking Federal indemnification for certain products and services. Under the Executive Order, as revised, the head of a Federal agency or department, other than the Secretary of Defense, considering a contractor's request for Federal indemnification for products or services that *have been* or *could be* designated as "qualified antiterrorism technologies" under the SAFETY Act must now consult with the Secretary of

Homeland Security and receive the approval of the Director of the Office of Management and Budget (OMB) before granting such a request. During this consultation, the Secretary of Homeland Security must advise the head of the agency or department whether use of the authorities provided to the Secretary of Homeland Security under the SAFETY Act would be more appropriate than Federal indemnification. If the head of the non-Defense agency or department determines that Federal indemnification is appropriate after such consultation, he must also receive approval from the Director of OMB before granting the contractor's request for Federal indemnification under P.L. 85-804. The revised Executive Order further states that the Secretary of Defense must only consider whether use of the SAFETY Act is appropriate before granting Federal indemnity for indemnification for products or services that have been or could be designated as "qualified antiterrorism technologies" under the SAFETY Act. Coordination with the Secretary of Homeland Security and approval by the Director of OMB is not required.

SAFETY Act Does Not Provide Protection from Pre-Terrorist Liability

The SAFETY Act does, in fact, provide significant protections to providers of countermeasures that receive certification under the Act. I must note, however, that to date, no such certifications have been granted for bio-defense countermeasures.

Significantly, Section 865(1) of the SAFETY Act notes that qualified anti-terrorism technologies may include technologies deployed for the purpose of

"limiting the harm such acts [of terrorism] might otherwise cause." The "harm" that may be caused by an act of terrorism clearly goes beyond the immediate effects of the act itself. An act of terrorism such as the attacks of September 11th or the October 2001 anthrax attacks trigger a number of immediate remedial and emergency responses to limit the resulting harm and deter follow-on attacks.

For example, immediately following the detection of anthrax in the offices of Senator Tom Daschle and Senator Patrick Leahy, Members of Congress and their staffs were treated with antibiotics and other prophylactic measures with the goal of limiting the harm that this act of terrorism could cause. Clearly, any injuries that might have been caused by the administration of these treatments, even though direct results of the act of terrorism itself could be directly traced to the act and the objective of limiting the resulting harm. Moreover, any claims brought as a result of such injuries would clearly be "arising out of, relating to, or resulting from an act of terrorism."

Limitations of the SAFETY Act for Bio-Defense Countermeasures

While the SAFETY Act can provide signification protections to a company, it has limitations in the context of countermeasures. Most significantly, the SAFETY Act does not provide compensation for those injured by qualified technology. Rather, the liability is removed as matter of law. That said, if the SAFETY Act were to be coupled with a limited compensation scheme bio-defense coutermeasures, liability would be addressed and victims could be made whole.

Moreover, the potential liability of a provider of anti-terrorist technologies that may allegedly cause injury PRIOR to a terrorist attack, such as a vaccine, are not currently addressed by the SAFETY Act.

In the legislative history of the Project BioShield Act of 2002, Congress stated that the Secretary of Homeland Security is "encouraged to designate [biodefense] countermeasures as 'qualified anti-terrorism technologies' as defined in section 862 of the Homeland Security Act." In the context of Project BioShield, there is great concern by makers of bio-terrorism countermeasures, diagnostics, and therapeutics that SAFETY Act protections do provide protection since liability frequently exists PRIOR to, in addition to following an act of terrorism.

For example, in the context of a diagnostic, a test kit for Anthrax exposure that may, perhaps, provide false positives would expose the manufacturer to tremendous - and likely insurable liability - thereby preventing widespread deployment, even if the diagnostic is the current state of the art.

Also, recognize that the research and development into these bio-defense measures as well as production, itself, may expose a company to potential liability given that both R&D and production may involve toxic materials, even if those toxic materials cannot possibly harm the public. For example, BIOPORT, the manufacturer of the Anthrax vaccine provided to the Department of Defense long before 9/11, was sued in Florida in the Fall 2003 for allegedly not preventing the Anthrax strain that killed the gentlemen in Florida in October 2001 from being stolen by terrorists. However, BIOPORT does not possess – nor has it ever

possessed - live strains of Anthrax. Moreover, the R&D companies that support the bio-defense industry that do routinely use these toxins, and yet, very rarely receive indemnification. This is just one example among many.

SAFETY Act Protections Should be Extended

Through minor changes to existing language, SAFETY Act protections should apply to technologies that mitigate against terrorist incidents, and such protections should attach if there is the POTENTIAL for a terrorist attack - not just after an act of terrorism occurs. Minor changes to the SAFETY Act, such as those proposed by Congressman Curt Weldon (R-PA) would easily address this issue and would be a significant step in providing the certainty necessary to stimulate the bio-defense market. (See attached).

Protections for Smallpox Vaccine Should be Expanded to All Bio-defense Countermeasures

The liability protections provided under the Homeland Security Act of 2002 (P.L. 107-296), and further expanded by the Smallpox Emergency Personnel Protection Act of 2003 (P.L. 108-20) for the administration of smallpox vaccines are, indeed, quite powerful. Though currently limited only to smallpox vaccine, the Congress should strongly considered extending this legislation to apply to providers of any countermeasure developed under Project Bioshield. Such a change would provide additional certainty on the issue of liability and would positively impact the creation of bio-defense countermeasures. I note that this provision is somewhat limited in that it is only triggered by declaration of the Secretary of Health and Human Services such that has been made regarding smallpox. Moreover, there are

significant questions regarding the precise scope of the protections afforded by this measure regarding the types of claims covered and the specific entities that are protected. Still, expansion of this measure to protect manufactures of countermeasures produced under Project Bioshield would be a significant improvement to the status quo.

Any legislation expanding the coverage of the liability protections afforded smallpox vaccines under the Homeland Security Act of 2002 must also expand the statutory language provided by the Smallpox Emergency Personnel Protection Act of 2003 to ensure identical treatment of all countermeasures with smallpox vaccine. It must also squarely provide liability protections for injuries alleged to be caused by non-negligent administration of the countermeasure (e.g., claims for breach of warranty and/or strict liability). Such legislation, coupled with expansion of the SAFETY Act, will provide the certainty necessary to develop a fully responsive bio-defense industry as quickly as possible and will provide a means for unintended victims to be compensated.

Existing Antitrust Measures Should Be Used to Address Bio-Defense Market Concerns

Turning to antitrust concerns surrounding Project Bioshield, the government's current homeland security efforts require various agencies, including the Department of Defense, to purchase a number of vaccines and other drugs to address multiple bio-terror threats. There are a limited number of companies capable of supplying such products to meet the government's growing needs. Further, no single company has the resources necessary to respond effectively to

multiple solicitations for such products. Moreover, the government market for these products is rather limited and uncertain, even with the passage of Project Bioshield. The limitations and uncertainties inhibit research, development and production of these products to satisfy the government's national defense needs that would normally be spurred through competitive market forces.

Defense Production Act Provides the Authority to Convene an Industry-wide Meeting

To address these challenges, the government has the express authority under the Defense Production Act (DPA) of 1950, as amended, 50 USC App. § 2361 *et seq.*, to convene a meeting of all relevant companies competing for government contracts that call for the development and production of certain vaccines for national defense purposes. Under such authority, the government may provide immunity from potential antitrust liability to a company that participates in a process with its competition, including meetings, the objective of which is to address issues of common concern to industry and the government. The government may, in exercising this authority, require competitors to act in collaboration or share information that otherwise could not be shared due to antitrust laws and regulations. The objective of this process would be to reduce or eliminate barriers that prevent companies from satisfying the government's national defense needs.

The DPA provides the government with the authority to permit companies to enter into certain agreements that could include potential competitors and would have the effect of altering competitive behavior for the development of bio-defense countermeasures -- activities which would otherwise violate the antitrust laws.

Under the DPA, the government may convene a meeting with all or some of the nation's bio-defense manufacturers to discuss the government's bio-defense procurement requirements. Topics at such a meeting may include issues of common concern such as market allocation, agreements that certain companies respond to specific solicitations, and/or required contract terms such as indemnification. If the DPA's statutory prescriptions are satisfied, the government's valid exercise of its DPA authority would provide complete protection against the operation of certain antitrust laws for the private-entity participants in this process.

The government has the authority to convene meetings and execute agreements creating what could be described as a "managed market" that fall under the DPA's exemption from the antitrust laws. Under this authority, parties could meet to discuss a proposed division of the total market for vaccines, countermeasures, and other drugs necessary to support homeland security, including possibly allocating drug research development and production contracts among potential competitors to avoid inefficient procedures associated with full and open competition in this context. Such a meeting might also address the need for certain contract provisions. The conduct of such meetings undoubtedly would require the sharing of information that could otherwise not be shared due to the operation of antitrust laws and regulations.

The DPA, and specifically 50 USC App. § 2158, expressly enable the creation of agreements among potential competitors, with the participation of the United States, the purpose of which is to manage the development and production of

defense-related goods and services and which agreements, but for this provision, might violate certain antitrust laws. Thus, the DPA will provide immunity[1] from any public or private antitrust action brought against a company that participates in such a meeting, provided that all of the technical elements outlined in the DPA have been met.

Essential to the operation of this exemption from the antitrust laws and regulations is the active participation of the United States which participation is described in considerable detail in the DPA itself. When conditions exist that directly threaten the national defense or its preparedness programs, the DPA authorizes the President to give antitrust immunity to rival contractors for the purposes of forming agreements to develop preparedness programs and to expand production capacity and supply beyond levels needed to meet essential civilian demand. William E. Kovacic, *Antitrust Analysis of Joint Ventures and Teaming Arrangements Involving Government Contractors*, 58 Antitrust L.J. 1059 (1989). Immunity against any civil or criminal action brought under federal antitrust laws or any similar law of any state may be conferred on any person that:

- Takes any action in the course of developing a voluntary agreement initiated by the President or a plan of action adopted under such agreement; or

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[1] While the statute itself refers to an "immunity" that is being conferred, we do not believe that the exemption amounts, literally, to an "immunity." Our reason for differing on the effect of the law is that a company would not be "immune" from an action brought by a private party or government, but rather could prevail in an antitrust action brought against it by showing that it had complied with a government supervised voluntary agreement or plan of action. See, 50 USC App. § 2158(j).

- Takes any action to carry out an approved voluntary agreement or plan of action initiated by the President; and
- Complies with the requirements of the DPA; and
- Acts in accordance with the terms of voluntary agreement or plan of action.

50 USC App. § 2158(j)(1).[2]

"Antitrust laws" for purposes of the DPA, have "the meaning given to such term in subsection (a) of the first section of the Clayton Act, except that such term includes Section 5 of the Federal Trade Commission Act to the extent that such section 5 applies to unfair methods of competition." 50 USC App. § 2158(b). That definition includes (by referencing the Clayton Act) the Sherman Act, 15 U.S.C. § 1, *et seq.*, which contains the antitrust prohibitions potentially applicable to the actions contemplated in this memorandum. The person seeking the immunity has the burden of persuasion to establish that each of the elements for receiving immunity under the DPA have been met. 50 USC App. § 2158(j)(3).

While immunity is not available if "the action was taken for the purpose of violating the antitrust laws," this provision does not present a problem for the government to achieve the overall objectives of the DPA. This language was

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[2] If a voluntary agreement or plan of action is accompanied by contracts with the United States that call for the conduct of the necessary research, development, and production, additional statutes exist which would protect against antitrust laws. See 10 USC § 2304(c) and 41 USC § 303©.

inserted during reauthorization of the DPA in 1991 as a "face-saving" measure for those legislators hesitant to reenact the antitrust immunity provisions of the DPA for fear of eviscerating existing antitrust law. Assuming that a company act in accordance with provisions of the DPA, and follows the government's directions in that regard, by definition, they are not acting for the "purpose" of violating antitrust laws.

Separately, the DPA provides immunity from liability, damages or penalties based upon acts or omissions "...resulting directly or indirectly from compliance with a rule, regulation or order issued pursuant to this act" even if such rule, regulation or order is thereafter held to have been invalid. This additional protection is operative here because the supervised agreements contemplated by the DPA would generally be effectuated by agency "rule" and "order" under the terms of the Act. This provision of the DPA is indeed written as a true immunity provision and, in our view, would bar a private antitrust action.

The Homeland Security Act of 2002 contains a provision that expressly references the antitrust exemptions of the DPA. The provision recites that the DPA confers antitrust immunity to participants in a "critical infrastructure protection program" established in accordance with the Homeland Security Act of 2002. This language was inserted in lieu of a stand-alone antitrust exemption which was ultimately considered unnecessary.

Moreover, the Federal Maritime Administration used the DPA for these purposes as recently as 1996. Under that voluntary agreement, the Department of Transportation convened a meeting with eligible U.S.-flag vessel operators to enter into a "Voluntary Intermodal Sealift Agreement" (VISA) to address the total sealift needs of the United States in the event of a national emergency. Specifically, the action was undertaken with the intention that "the participants that are party to a VISA will provide capacity to support a significant portion of surge and sustainment requirements in the deployment of U.S. military forces." 60 FR 54144 (October 19, 1995). While the DPA was used to allocate market-share on at least fifty occasions during the Korean War,[3] the VISA program is the most recent example of the governments use of the DPA for these purposes. The VISA program remains in effect today. These examples demonstrate that the DPA is available to protect participants from antitrust liability for government-sponsored agreements to divide market share among competitors.

As a prerequisite to establishing a voluntary agreement under the DPA, the President (or his approved designee) must find that "conditions exist which may pose a direct threat to the national defense or its preparedness programs." 50 USC App. § 2158(c)(1). By Executive Order 12919, dated June 3, 1994, the President has delegated this authority to the heads of each federal department or agency. E.O. 12919, Part V, Sec. 501. Once appointed, the President's designee (defined as the

[3] See generally, Harold L. Schilz, *Voluntary Industry Agreements and Their Exemptions from the Antitrust Laws*, 40 Va. L. Rev. 1 (1954).

"sponsor" by the governing regulations) must consult with the Attorney General and the FTC not less than 10 days before attending a meeting discussing any proposal to develop a voluntary agreement. In addition, the sponsor must have received prior approval from the Attorney General to have such a meeting. 50 USC App. § 2158(c)(2).

Regulations providing the standards and procedures by which voluntary agreements may be developed are found at 44 CFR 331.1-4. In accordance with these regulations, any sponsor that wishes to develop a voluntary agreement shall submit to the Attorney General and the Director the Federal Emergency Management Agency (FEMA) a proposal that includes statements regarding:

- The purpose of the agreement;
- The factual basis for making the finding that "conditions exist which may pose a direct threat to the national defense or its preparedness programs;"
- The proposed participants in the agreement; and
- Any coordination with other federal agencies accomplished in connection with the proposal.

Upon a finding that the prerequisites for initiating a meeting to discuss a voluntary agreement under the DPA have been met, "the President [or the approved sponsor] may consult with representatives of industry, business, financing,

agriculture, labor, and other interests...[to facilitate the creation of]...voluntary agreements and plans of action to help provide for the defense of the United States through the development of preparedness programs and the expansion of productive capacity and supply beyond levels needed to meet essential civilian demand in the United States." 50 USC App. § 2158(c)(1).

Voluntary agreements may only be developed with the direct involvement of the Attorney General, the Chairman of the FTC, and the Director of FEMA, or their designees. The sponsor of the agreement must serve as the chairman of any meeting discussing proposed voluntary agreements. The sponsor must ensure that notice of the time, location, and nature of any meeting discussing a proposed voluntary agreement is published at least seven day in advance. All interested persons must be invited to submit written data and views concerning the proposed voluntary agreement, with or without the opportunity for oral presentation. In addition, all interested persons must be invited to attend any meeting discussing the proposed agreement, unless the chairman finds the subject of the meeting is protected under the Freedom of Information Act (FOIA). Finally, a full and verbatim transcript must be prepared for any meeting discussing the proposed agreement. This transcript must be provided to the Attorney General, the FTC, and Congress, and be made available for public inspection and copying, subject to FOIA. 50 USC App. § 2158(d); 44 CFR 332.2.

Voluntary agreements are executed through a "plan of action," which may include the conduct of research and development contracts. Such a plan may also

include contracts for the production of goods and services or other actions as agreed to by the parties to the voluntary agreement and the government.[4]

Voluntary agreements, and any plans of action contemplated by such agreements, become effective when the sponsor certifies, in writing, that the agreement or plan is necessary and the sponsor submits the agreement or plan to Congress. In addition, the Attorney General (with consultation from the FTC Chairman and the FEMA Director) must find, in writing, that the purpose of the action "may not reasonably be achieved through a voluntary agreement or plan of action having less anticompetitive effects or without any voluntary agreement or plan of action and publishes such finding in the Federal Register." 50 USC App. § 2158(f)(1); 44 CFR 332.1(b)(2); E.O. 10480, §§ 101 & 501(a).

Voluntary agreements and plans of action contemplated by such agreements expire two years from the effective date and may be extended upon certification or finding by the sponsor and the FEMA Director that such extension is appropriate. 50 USC App. § 2158(f)(2). The Attorney General may terminate or modify a voluntary agreement, in writing, after consultation with the FTC Chairman. The sponsor of the agreement, with the concurrence of the FEMA Director, may terminate or modify a voluntary agreement, in writing, after consultation with the Attorney General and the FTC Chairman. Any person who is a party to a voluntary

[4] The term "plan of action," as defined by the DPA, means "any of 1 or more documented methods adopted by participants in an existing voluntary agreement to implement that agreement." 50 USC App. § 2158(b)(2). A plan of action is issued by the government with the express agreement and cooperation of all of the parties to the voluntary agreement.

agreement may terminate his participation in the agreement upon written notice to the sponsor. No antitrust immunity shall apply to any act or omission occurring after the termination of the voluntary agreement or any act or omission that is beyond the scope of the agreement. 44 CFR 332.5.

If the technical elements of the DPA have been satisfied, competitors may meet to discuss with government the formation of voluntary agreements with its potential competitors that could have the effect of dividing the markets or developing common contract terms for the countermeasures to be developed. Such voluntary agreements may include a plan of action to be issued by the sponsoring agency that permits, among other things, division of market share and/or assignment of certain contracts among participants to the agreements. Again, all such meetings, voluntary agreements, and plans of action must comply with all of the requirements of the DPA to be afforded protection from antitrust laws and regulations.

I note that this authority exists today - and has since 1950. Congress should consider whether use of this authority would enable HHS to address many of the issues facing companies that are resistant to otherwise participate in this market. Clearly, simply convening a meeting under the authorities of the DPA to discuss this issue would most certainly stimulate interest and facilitate discussion with a far broader number of entities than are expressed interest in the bio-defense interest today.

Thank you again to Chairman Gregg, Chairman Hatch, Senator Kennedy and Senator Leahy and members of the Committees for your attention to this critical issue. I welcome your questions.

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OPENING STATEMENT OF SENATOR MICHAEL B. ENZI

COMMITTEE ON HEALTH, EDUCATION, LABOR, AND PENSIONS
JOINT HEARING WITH THE COMMITTEE ON THE JUDICIARY

"BioShield II: Responding to an Ever-Changing Threat"

OCTOBER 6, 2004

Protecting America from bioterrorism will require the best efforts of both government and the private sector, so I commend Chairmen Gregg and Hatch for calling this hearing to see what more needs to be done to make America as safe as possible from this threat.

The legislation to enact President Bush's Project Bioshield, which Congress passed into law in July, is an important first step toward safeguarding our homeland and our citizens from a bioterror attack and its aftermath. I am proud to have cosponsored that legislation and am committed to seeing that the law improves our biodefense capabilities. My only regret is that it took more than a year for the full Senate to approve this bill after the HELP Committee reported it to the floor with unanimous support.

Looking forward, it is critical for these two committees to work together to build upon Project Bioshield. Project Bioshield was never intended to address all of the obstacles to the development of bioterror countermeasures. It was intended simply to establish a stable and guaranteed source of federal financing for the purchase of countermeasures developed by private industry, since most of these products don't have other significant commercial applications.

Now that we have established this financing mechanism, it's time that we address the other roadblocks that impede our progress on bioterrorism countermeasures. Chairman Hatch and Senator Lieberman have developed a bill that aims to address a wide variety of outstanding concerns that must be addressed, from liability protections to intellectual property incentives. I look forward to hearing Senator Lieberman discuss his bill today.

Senator Lieberman will testify today that we need to engage the biotechnology and pharmaceutical industries in our efforts to spur the development of bioterror countermeasures. I wholeheartedly agree with Senator Lieberman that we will not be able to address fully this threat without tapping the ingenuity that resides in these innovative industries. We need their input and involvement as we take the next steps toward protecting America from bioterrorism.

Again, I thank the Chairmen and the Ranking Members as well for coming together to refocus these committees on our biodefense capabilities. I look forward to working within the HELP Committee and with the Judiciary Committee as we build a strong national biodefense.

Aventis Pasteur

CHRISTINE GRANT, ESQ.
VICE PRESIDENT,
PUBLIC POLICY AND GOVERNMENT RELATIONS

TESTIFYING ON BEHALF OF
AVENTIS PASTEUR

BEFORE THE SENATE JUDICIARY
COMMITTEE AND HELP COMMITTEE
October 6, 2004

REGARDING PROJECT BIOSHIELD

October 6, 2004

Aventis Pasteur

Mr. Chairman and Members of the Committee, it is an honor for me to testify before you today regarding Project BioShield and its likely impact in bringing private sector talent and investment into our nation's bio-defense effort.

I appear before you today representing one company – Aventis Pasteur. Aventis Pasteur is the largest company in the world devoted entirely to vaccine research, development, and manufacturing. Aventis Pasteur produces approximately 1.4 billion doses of vaccines annually, making it possible to protect 500 million people across the globe. The company offers the broadest range of vaccines, providing protection against 20 bacterial and viral diseases.

The company manufactures influenza vaccine and several other vaccines at its United States headquarters in Swiftwater, Pennsylvania. Over the years, Aventis Pasteur has had enormous successes, including the first application of conjugate vaccine technology and the licensing of the first infant acellular pertussis vaccine. While being involved in vaccine development, Aventis Pasteur also routinely supplies vaccines and biologicals needed by both civilian and military populations, including vaccines against tetanus and diphtheria, yellow fever, Japanese encephalitis, meningitis, typhoid fever, and influenza to name a few.

Aventis Pasteur has partnered with the Federal government in times of peace as well as in times of conflict. Immediately following the attacks on the World Trade Center on September 11, 2001, Aventis Pasteur worked closely with metropolitan New York and New Jersey public health and city officials to donate 50,000 doses of Tetanus Diphtheria Toxoids Adsorbed vaccine to the relief efforts. Most recently in 2002, Aventis Pasteur demonstrated this commitment by donating approximately 85 million doses of smallpox vaccine to the Federal government's emergency preparedness stockpiles. The company has always supplied the United States military with needed vaccines, including those being used today by our troops fighting in Iraq. The company has responded to more than one Federal request for proposal for bio-defense measures, and therefore, has current experience on this subject. Finally, Aventis Pasteur has been a leading participant in the Global Polio Eradication Initiative, a partnership created to deliver polio vaccine to every child under five, worldwide. Aventis Pasteur has donated a total of 120 million vaccine doses since 1997 under this initiative.

Aventis Pasteur

Aventis Pasteur supports the objectives of Project BioShield to expedite the Federal government's ability to contract for needed bio-defense products and to provide important certainty to applicants that money will be available to meet contractual commitments over a period of years. Development and production of complex medical and biological products requires a number of years under the most favorable circumstances and multi-year contracting needs to be available. Passage of this legislation was a significant step forward in preparing the Nation to meet the challenge of defending against bio-terror.

While we recognize that the legislation includes significant positive steps toward developing the nation's bio-defense capabilities, Congress must ensure that Project Bioshield is properly implemented by the Department of Health and Human Services (HHS). Moreover, Congress can significantly improve the law in the area of liability protection and contracting reform by amending the law as part of Project Bioshield II. These changes will dramatically strengthen Project BioShield and help ensure that its most important objective -- to ensure the efficient development of needed safe and effective bio-defense products -- is achieved.

HHS must ensure that key provisions of Project Bioshield are implemented to their Fullest

During the Congressional debate on Project Bioshield, Aventis Pasteur strongly supported the need to provide for the possibility of the Federal government entering into agreements (including contracts, grants, cooperative agreements, and "other transactions") that permit the HHS Secretary to contract with bio-defense companies for research and development and manufacturing/production under one agreement. Reports supporting the House version of Project Bioshield issued by all three Committees of jurisdiction makes clear this was the unquestionable and worthy intent of Congress.

A company like Aventis Pasteur, which not only does research and development, but emphasizes the reliable manufacture of millions of doses of vaccines, needs the certainty that satisfactory completion of research and development will lead to a manufacturing agreement. HHS must take the steps necessary to ensure that Congressional intent is fully realized as it manages the regulatory process.

Similarly, Project Bioshield provides HHS with broad steamlined procurement authorities to ensure that the contract process is expedited with as little burden to commercial contractors as possible. This includes significantly reducing the burdens on prospective contractors by limiting the applicability of certain procurement regulations to eliminate the need to alter their commercial business practices significantly in order to produce bio-defense countermeasures for the Federal government. In accordance with Congressional intent, HHS must ensure that Project Bioshield is implemented to ensure the "Request for Proposal" process makes maximum use of these streamline authorities.

The need for Project Bioshield II

Project Bioshield was a significant step in the right direction. Congress and the Administration should be commended for their leadership; however, several issues must be addressed in BioShield II to enable the vaccine industry to more effectively and efficiently develop safe and effective bio-defense countermeasures. Passage of Project Bioshield II, which should address these issues, would send a significant signal that the Federal government is, indeed, serious about ensuring the nation is protected.

Bioshield II should expressly provide for the authority limit the extent of liability for any contractor engaging in research, development, and production of BioDefense countermeasures

The issue of potential liability for any entity that provides, or performs research and development related to, bio-defense countermeasures absolutely must be addressed in order to stimulate private sector interest in entering into agreements for such countermeasures. For example, the absence of liability protection was a major obstacle in the recent procurement by NIH for development of the next-generation of Anthrax vaccine and continues to be a major hurdle for our company. We would try to obtain commercial insurance, but the practical reality today is that it is unlikely to be available for projects of this nature. Project Bioshield is silent with respect to addressing liability.

Aventis Pasteur

The passage of the Homeland Security Act of 2002 radically altered the way the United States will go about promoting the development of technologies designed to counter against a terrorist attack. This was accomplished by means of the SAFETY Act (which stands for the "Support Anti-Terrorism by Fostering Effective Technology."). Under the SAFETY Act, a wide array of legal protections are now available to qualified sellers, vendors, subcontractors, and buyers of anti-terror technology products and services, including bio-defense countermeasures. Such protections take the form of drastically reduced liability in the event an anti-terror technology fails and damages or casualties result.

Products and services that are developed following an act of terrorism might also be considered to be deployed in defense against, in response to, or recovery from an act of terrorism and thus be eligible to receive the protections of the SAFETY Act. In the context of pharmaceutical products, this would encompass giving SAFETY Act coverage to vaccines or drugs that were designed to counter a biological agent that was previously used in a terror attack. Indeed, we have been advised by counsel that there is a very strong argument to be made that pharmaceutical products manufactured in part as a response to the 2001 anthrax attacks are eligible for SAFETY Act protection. Providing SAFETY Act coverage to pharmaceutical products currently being manufactured is in line with the purposes and the text of the SAFETY Act, as it was explicitly written to provide protection for technology and services deployed in "response" to an act of terrorism.

In response to the 2001 anthrax attacks, a number of pharmaceutical products are being prepared and deployed in order to reduce the vulnerability of the United States to another anthrax attack. Since those products are in "response" to an act of terrorism, there should be no doubt that they are eligible for SAFETY Act protections, and extending coverage to them is in line with the intent of the SAFETY Act. For instance DHS has explicitly stated that the success of the SAFETY Act depends "upon encouraging Sellers to develop new and innovative technologies to respond to the ever-changing threats to the American people." 68 Fed. Reg. 59,692 (2003). It would be in line with that directive then to extend protections to pharmaceutical products that are developed and deployed specifically to respond to the threat demonstrated by a terrorist attack that previously occurred.

Recognizing that the protections of the SAFETY Act already extend to pharmaceutical products is an important step in fostering homeland security. More, pharmaceutical products that are developed and manufactured after an act of terrorism has occurred should also be eligible for protection under the SAFETY Act. The perfect example there would be vaccines and drugs developed, manufactured and deployed in the wake of the 2001 anthrax attacks. Such products should be eligible for SAFETY Act protection as they are being deployed in response to an event that represents a triggering act of terrorism. That position is logical in light of the liability risks faced by pharmaceutical companies as well as the risks faced by the United States as a whole if it is unprepared for a new biological attack.

It is also worth noting that both the Secretary of Health and Human Services and the Secretary of Homeland Security currently have the authority to provide for Federal indemnity to private entities engaging in research, development, and production of biomedical countermeasures under Public Law 85-804. However, use of such authority is extremely rare. Also, in March 2003, President Bush revised Executive Order 10,789 governing use of the authority to provide for indemnity under Public Law 85-804 in the context of anti-terrorism technologies such as those to be developed under Project Bioshield. While HHS has been proactive in recognizing the need to consider use of the SAFETY Act, it must ensure that Federal indemnity remains available, where appropriate, as was the intention of both the law and the Executive Order.

Finally, while HHS is currently using its authority under Public Law 85-804 in very limited circumstances, it is our best understanding that the agency is not providing such indemnification/liability protection until a contact is awarded – and will not guarantee that this protection is forthcoming as part of the award process. This is not the intention of the law nor is it the practice of other agencies that have the authority to provide such liability protection to contractors. Congress should ensure, through Project Bioshield II, that HHS applies this provision in a way that was intended by both the law and regulations implementing Public Law 85-804.

Aventis Pasteur

Moreover, this issue places a potential contractor in the untenable position of having to perform "bare" and assume an unusually high legal risk, or refuse to perform, and be found in breach. Once a contract is awarded, a contractor has no meaningful negotiating strength, and is reliant on the contracting agency. In essence, we are reallocating labor, capital and resources and investing in high-risk products without sufficient assurance that liability protection will be available. It is essential that we fully address this situation.

Bioshield should provide for express authority to enter into agreements that resemble fully negotiated commercial transaction

Aventis Pasteur recommends that Project Bioshield be amended to expressly permit the Secretary of HHS to enter into "other transactions" in order to provide the maximum degree of flexibility suggested by the proposed legislation. "Other transaction" authority will permit agreements between HHS and industry that more closely resemble a fully negotiated commercial transaction. Similar authority has been provided to both the Department of Defense and NASA and has resulted in numerous success stories including, most recently, the "Predator" program in use in Afghanistan and Iraq today.

While HHS received "other transaction" authority, generally, for anti-terrorism activities under Title XVI of the Defense Authorization Act of 2004, HHS has taken no steps to implement use of this authority inside or outside the context of Project Bioshield. Moreover, under this legislation, HHS is required to receive permission from the Director of the Office of Management Budget before entering into such an agreement. Providing HHS with explicit authority to enter into "other transactions" without additional approval would allow HHS to maximize private sector participation in ensuring bio-defense measures are deployed and developed as broadly and quickly as possible.

Mr. Chairman, thank you for the opportunity to testify on this tremendously important issue. Aventis Pasteur has been and remains committed to contributing to our nation's common defense. I will be pleased to respond to any questions from members of the Committee.

Testimony of Patricia Greenberg, RN, on behalf of the Service Employees International Union, AFL-CIO, on Bioshield II and related Senate Bill 666, the Biological, Chemical, and Radiological Weapons Countermeasures Act , before the U.S. Senate HELP and Judiciary Committees, October 6, 2004

Good morning Committee Chairmen Gregg and Hatch, Ranking Members Kennedy and Leahy, and other Members of the Senate HELP and Judiciary Committees.

My name is Patricia Greenberg. I have been a registered nurse for 23 years. I have worked as an operating room and intensive care nurse in Syracuse, New York, and I am the Executive Director of the 27,000 member New York State Nurse Alliance SEIU 1199.

On behalf of Service Employees International Union, thank you for this opportunity to testify. I also thank the sponsors of Senate Bill 666, for honoring Kathy Nguyen by mentioning her name on page 2 of the proposed legislation. Kathy was a member from my local union who died from her exposure to anthrax contained in a contaminated letter.

SEIU is the nation's largest organization representing health care workers, with over half of our 1.7 million members comprised of nurses, doctors, EMTs, laboratory technicians, orderlies, dietary workers, laundry workers, environmental services workers, and other occupations within the health care sector. Many of these employees work in occupations that would likely be defined as "first responders" in the event of a terrorist attack.

As nurses, we want to do everything in our power to respond to, treat and care for any patient who may be a victim of a terrorist event.

This is why we have reviewed Senate Bill 666 with great interest. We are supportive of the broad principles of the legislation to encourage the development of new countermeasures to protect all of us from such threats.

In particular we have noticed how Senate Bill 666 is quite comprehensive in protecting the drug and other biotech companies who produce countermeasures from liability.

In sharp contrast, we are alarmed that there is no mention of providing protections either from injury or from liability for the courageous volunteers working on the front lines to protect our national security, if they suffer as a direct result of the implementation of any of these countermeasures.

Frankly, we have been down this road before. The Homeland Security legislation that passed in 2002 provided blanket liability protections for smallpox vaccine manufacturers and everyone involved in administering this vaccine, with no protections afforded to frontline workers, their patients or the public. We fear that the legislation before us today mimics many of the same serious flaws that were contained within the Bush Administration's failed smallpox vaccination program.

This bill is even more troubling when you recognize that it is premised on the expectation that there won't be time to do full safety testing on these countermeasures. As a result, we fear that once again nurses and other first responders will be hesitant to roll up their sleeves when they learn of this bill's deficiencies.

If we are protecting the manufacturers that create the countermeasures and the health facilities that implement these countermeasures from liability, we need to be sure that the first responders who will be receiving and administering the countermeasures to others are also protected in the event of adverse reactions.

We know that the best countermeasures in the world will not be effective if health care workers and their patients do not have confidence in the safety of the countermeasures, and if those injured can expect no more than a "Get Well" card from their elected leaders.

You may recall the televised announcement by President Bush in December 2002 to initially vaccinate 500,000 health care workers against smallpox within thirty days, followed by 10 million more public safety workers within six months.

What you may not have been aware of was a public meeting convened by the CDC more than six months earlier. At that meeting, a number of organizations identified a wide range of serious gaps in patient and worker protection in the program that we all hoped that CDC would address beforehand so that the program would succeed. Unfortunately, Dr.

Gerberding stated at a press conference after our meeting that the Administration did not have time to address these concerns.

The result today is that less than one half of one percent of the original goal of ten million workers have been vaccinated. We hope that Senate Bill 666 can do better and not repeat the failures of the smallpox vaccine program that led the Washington Post to describe the effort in an editorial a year ago this past July as a "fiasco."

In our judgment, it is only fair that nurses, health care workers, and other first responders, who are putting their lives on line to protect our national security have the necessary safeguards in place to care for themselves, their patients, and the public at large.

We continue to be dismayed by the lack of overall preparedness in many health care facilities as they confront potential threats.

To better prepare ourselves, over a year ago my union launched a program in collaboration with leading medical centers, and we have already trained thousands of emergency room staff, EMTs and other first responders to confront the wide range of emerging health threats from SARS and avian flu, to terrorists' agents.

We know that HRSA has already distributed well in excess of $1 billion dollars to hospitals for preparedness, yet there has been no criteria issued by HRSA, OSHA or DHS on how the monies should be spent. The result in many instances has been the purchase of much equipment of dubious value hidden away in closets, without adequate staff training and hands-on experience.

If we are serious about protecting our healthcare workers and first responders, handing out billions of federal dollars with no requirements from HRSA, OSHA or DHS on what employers need to be doing is a recipe for massive misspending.

In one of the more egregious examples of the contradictory nature of what is happening regarding overall terrorism preparedness, this past December federal OSHA killed their final tuberculosis standard; the one standard that would have served as a proxy to protect health care workers from other airborne threats, including airborne weapons of mass destruction. This was

followed by actions last month by the US House that added an appropriations rider to prevent OSHA from enforcing a life-saving provision of the agency's respiratory standard requiring employers to conduct annual tests to prevent respirators from leaking.

We sincerely hope that the Senate can do better for first responders with the legislation now before you, and therefore respectfully offer the following suggestions for improvement in this important piece of legislation:

We believe that a comprehensive terrorism countermeasures prevention program that protects health care workers, patients, and their families in advance of a terrorist event would:

- Include a requirement that health care workers and other first responders be fully educated about the benefits and risks of any countermeasure before implementation;

- Ensure that workers have the freedom to decline newly produced vaccines or other countermeasures that have not been sufficiently tested without being discriminated against at work. This language could be modeled after similar protections afforded workers under the OSHA Bloodborne Pathogens Standard;

- Provide free and confidential medical screening for anyone volunteering in any vaccine or drug trial involving countermeasures to assure those with preexisting medical conditions are not exposed;

- During the piloting and implementation of countermeasures, inform patients of the risks and benefits, and the safeguards that have been put into place to protect them;

- Require the monitoring of volunteers who receive any countermeasures so that any adverse effects can be adequately tracked by the federal government so that potential risks can be fully evaluated;

- Ensure that any health care worker or other first responder who volunteers and gets sick due to participating in any countermeasures does not face loss of income if they can not work as a result;

- Provide free medical care to those who volunteer and are injured or made sick by any countermeasures;

- Require that health care workers and other first responders be provided with an explanation of any new job duties resulting from the implementation of the countermeasure(s); and

- Contrary to how the smallpox vaccine was administered, require that any new vaccines or other medications that utilize needles or other sharp instruments, be administered with needles with integrated safety features as required under the federal Needlestick Safety and Prevention Act of 2000.

Thank you, and I would be glad to respond to any questions.

GPhA
GENERIC PHARMACEUTICAL ASSOCIATION

Testimony Before the
Joint Senate Judiciary and H.E.L.P. Committee
Hearing On S. 666, BioShield II

October 6, 2004

Testimony of Kathleen D. Jaeger
President & CEO
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GPhA Testimony: Joint Senate Judiciary and H.E.L.P. Committee Hearing On S. 666, BioShield II

October 6, 2004
Testimony of Kathleen D. Jaeger
President & CEO
Generic Pharmaceutical Association

Chairman Gregg and Ranking Member Kennedy, Chairman Hatch and Ranking Member Leahy, I am Kathleen Jaeger, President and CEO of the Generic Pharmaceutical Association. On behalf of GPhA and its members, we thank you for this opportunity to testify on ways we can partner with you to strengthen our response to bioterrorism threats against America.

I want to assure Members of both Committees, as well as all Americans, that the generic pharmaceutical industry stands ready to serve in any way to help our nation address the threat of terrorism. The members of the generic pharmaceutical industry represent a powerful production engine that can be – and is being -- brought to bear to respond to and defend against bioterrorism attacks. Our ability to manufacture and distribute safe and effective pharmaceutical products is unmatched. We are here to support the Administration, the Congress, first responders, and the American people in the preparation for an event or in response to biological, chemical, or nuclear assault.

In my testimony today, I plan to talk briefly about the strong foundation program set forth in BioShield I and identify the provisions of S. 666 that could, if enacted, build on that strong foundation in a positive fashion. I also will address the four provisions of S. 666 which would have unfortunate negative spillover effects on the health care system as a whole, potentially resulting in tens of billions of dollars in needless spending.

GPhA is committed to working with you to strengthen BioShield I in ways that will accelerate research, development and manufacturing of novel countermeasure agents[1], as well as diagnostic and environmental warning/detection devices. We believe that this committee can and should strengthen BioShield I by considering the addition of certain incentives, such as needed product liability protections, expanded tax incentives, additional federal research dollars, and fast tracked FDA review of drug and device applications.

GPhA, however, believes that four provisions currently included in S. 666 will:

1) reverse current law that enables the timely introduction of generic drugs;
2) create a "wild card exclusivity" that will unnecessarily cost healthcare providers and consumers billions of dollars;

[1] The term "novel" as used throughout this document means new molecular entities and new and modified vaccines.

3) excessively and unnecessarily increase market exclusivity on nearly any drug that can be broadly defined as a "countermeasure" --- again adding unneeded and unsupportable costs; and
4) create open-ended patent extensions for broadly defined countermeasures – that may or not be developed and manufactured for the government.

We believe that legislation to ensure that America is fully prepared for any threat must not become the vehicle for special interest proposals that will throw the competitive pharmaceutical market out of balance. We support efforts to strengthen BioShield I in a manner that meets the dual challenge our nation currently faces. First, we must preserve the security of our nation in a time of terrorist threat. Second, we must simultaneously ensure that America's healthcare system can meet the immediate need for more affordable medicine for all consumers. Both of these challenges must be kept in balance, as we seek to further strengthen BioShield I.

A. Generic Industry Background

To provide context to our testimony, GPhA represents manufacturers and distributors of generic pharmaceutical products, manufacturers and distributors of bulk active pharmaceutical chemicals, and suppliers of other goods and services to the generic pharmaceutical industry. In the 20 years since the enactment of the Hatch-Waxman Act, generic drugs have come to be widely accepted as the therapeutic equivalents of brand-name drugs, and the resultant savings have totaled hundreds of billions of dollars.

More than 51% of the American prescriptions last year were filled with affordable generics; yet, generics represent less than 8% of the total pharmaceutical expenditures for last year. Patients rely on generics to improve their lives, and the nation relies on generics to help keep U.S. health care affordable.[2] Among the many products that our members produce are generic antibiotics that CDC has identified as drugs of choice for treating many of the diseases listed as possible targets for countermeasures. And because we are leading producers of pharmaceutical products based on number of doses manufactured each year, our member companies can and should be considered as a valuable resource in responding to any widespread bioterrorist threat to Americans.

I. Building on the Strengths of BioShield I

Since the terrible events of September 11th three years ago, and the subsequent introduction of anthrax spores into the U.S. mail, the nation has been shocked into recognition of our vulnerability in the face of possible terrorist incidents involving biological, chemical, and nuclear materials or agents. There is general consensus that our arsenal of vaccines, diagnostic tools and other biomedical countermeasures to combat such threats is seriously deficient.

[2] Generic pharmaceutical products are used to fill over one billion prescriptions each year, yielding savings of tens of billions of dollars to consumers, insurers, businesses, and government.

The enactment of BioShield I (P.L. 108-276) in July of this year was a watershed event in the nation's preparation to meet such threats. This landmark legislation, proposed by the President and sponsored by Senator Gregg, gives the federal government many of the tools needed to stimulate research, research on, and development and production of novel biomedical countermeasures. It enables the Secretary of HHS to expedite the procurement and simplify the acquisition of countermeasures, and empowers the Secretary to declare emergencies and take steps to get needed countermeasures to affected members of the public. The new law enables the Secretary to make available during emergencies specific drugs and other biomedical countermeasures that have not yet been approved for general consumption.

In many ways, Project BioShield exemplifies what can result when the federal legislative process works best. It is well crafted and carefully thought out. It establishes direct accountability to designated Congressional committees and mandates a follow-up GAO report. This legislation emphasizes the best features of government procurement and contracting in preparing the nation to meet biomedical threats. And, already, we are seeing representatives of the pharmaceutical industry, the federal government and academia responding to the new law's incentives and call for action.

Nonetheless, even prior to the enactment of Bioshield I, questions arose about possible shortcomings, especially with respect to product liability concerns associated with necessary biomedical countermeasures. Fortunately, S. 666, the legislation before you today, includes several key provisions that could potentially strengthen Project BioShield.

II. The Promising Provisions of S. 666 (Extension of Bioshield I)

We believe that four provisions of S. 666 look promising in that they may offer significant incentives for enhancing our readiness as a nation.

First, S. 666 responds to onerous product liability concerns that could hinder product development and production. The legislation as proposed would extend the protections of the Smallpox Emergency Personnel Protection Act of 2003 to the approved countermeasures under this legislation. Such a measure could help reassure both investors and manufacturers by reducing their legal risk from involvement at all stages in the development, production, and distribution of qualified biomedical countermeasures.

Second, S. 666 provides additional tax credits and tax incentives to encourage investment in countermeasures. This provision could provide more attractive incentatives to small to medium size companies, as well as help attract the venture capital for smaller start-up firms who could research, develop and produce novel countermeasure agents.

Third, S. 666 provides for FDA "fast track" review of countermeasures falling under the agency's jurisdiction. This provision will help expedite the review, approval and availability of needed countermeasures in a timely fashion.

Finally, S. 666 establishes a Terror Weapon Countermeasures Purchase Fund with authorization for expanded funding for procurement of countermeasures. This provision could furnish pre-production payments to those developing countermeasures, yielding fiscal stability which is of a particular concern of smaller companies.

Each of these provisions builds on the strong foundation laid by Project BioShield. Each is clearly linked to promoting the development and production of needed biomedical countermeasures. None of these has any apparent negative consequences for other actors in the health care or security arenas.

It is important to note that when S. 666 was introduced, BioShield I had not yet been enacted. In the interim period, it has become clear that minor revisions will strengthen its implementation. GPhA encourages Congress to consider extending Bioshield I to include one or more of these promising concepts.

II. The Harmful Provisions of S. 666

Four of the provisions contained in S. 666 as proposed would create substantial opportunities for special interests to game the system and would establish loopholes that will harm, rather than help, American consumers. In fact, many of these loopholes previously have been proposed by special interests over the past 20 years in an effort to delay or prevent generic competition for brand name drugs. Each time, these proposals have been defeated and the best interests of American consumers have prevailed. In addition, given that many barriers to the more timely introduction of generic drugs were closed as part of the Medicaid Reform Act of 2003, it is alarming that they now appear attached to legislation whose goal is and should be American preparedness.

GPhA believes that Congress cannot allow the approval of S. 666 because the bill is overly broad in that fails to: (1) require research on, and development and manufacturing of novel countermeasure agents for purposes of receiving incentives under the bill; (2) set research, development and manufacturing priorities for countermeasure agents; and (3) require deliverables either in the form of disseminating the research or producing product for stockpiling. Moreover, S. 666 includes four seriously harmful provisions that will penalize consumers to the tune of billions of dollars in lost pharmaceutical savings, in the name of preparedness.[3]

These four provisions alone will create devastating effects on the current healthcare system by: undermining the balance of Hatch/Waxman Amendments; increasing the incentive for brand pharmaceutical manufacturers to participate marginally in bioterrorism research while reaping "wild card exclusivity" for any drug of their choosing, whether related to bioterrorism or not; and/or providing patent extensions and exclusivity that are ill-advised and open-ended.

[3] GPhA is analyzing the antitrust provision and its implications as set forth in S. 666, and would be pleased to provide input on this provision in the near future, upon request.

There is no question that these four provisions will generate higher drug costs. They will impede access to affordable generics. They will pose major economic challenges to already overburdened private and public third party payers, including employers, insurers, consumers and such government programs as Medicare and Medicaid. The damage to an already fragile healthcare environment could hardly be more ill-timed, given growth in the number of uninsured Americans, serious deficits in the Medicare and Medicaid programs, soaring health insurance premiums, and the numerous other crises facing the healthcare system.

Let me discuss each of these provisions individually.

A. Generic Industry Penalty Provisions

First, S. 666 contains ***two generic industry penalty provisions*** which strike at the heart of the Hatch-Waxman Act – legislation that created the generic pharmaceutical industry and permitted the generation of tens of billions of dollars in prescription drug savings every year.

The first generic penalty that threatens our nation's healthcare system would grant a brand product a five-year market extension added to a patent term or other exclusivities when a generic company files an application containing the requisite patent certifications in accordance with the Hatch-Waxman Act. This provision essentially repeals the Bolar Amendment, which for two decades has enabled generic manufacturers to develop a generic in advance of the expiration of the patents on a brand product as long as this use is reasonably related to meeting FDA approval requirements. Bolar allows generic manufacturers to develop their product so that it can be marketed immediately upon the expiration of the brand product patents.

If the filing of a generic product application is allowed to trigger an automatic market extension, the introduction of competitively priced generic drug will be delayed by five years. This generic penalty provision will condemn American consumers to the payment of higher brand prices with little benefit to bio-terrorism preparedness. Yet lost savings is not a prerequisite for ensuring America's safety against bio-terrorism threats.

In addition, another penalty that would be imposed under S. 666 will penalize generic manufacturers who attempt to challenge the patents of brand-name manufacturers and fail. Today, if a patent challenge fails in court, the brand product continues to be patent protected. Under S. 666, the failure by a generic company to succeed in a patent challenge will have the additional effect of granting the brand company an unearned extension of five years of market exclusivity. The intent of the patent challenge component of Hatch/Waxman was to create a mechanism for challenging suspect patents, with consumers receiving the benefit of immediate savings if the generic company prevailed. Taxol is the best example of the value of the patent challenge process. By proving that the patents protecting this product were invalid, the generic industry delivered more than $11 billion in savings to American consumers. Not only would this penalty create a significant disincentive for generic patent challenges, it would penalize consumers.

The following two examples clearly define the penalties generic companies will face, and for which the public will have to pay. It must be understood that the trigger, the filing of a generic application with patent certification, is required by federal law for all generic applications. Therefore, the mere filing of a generic product application under current law is an automatic trigger for exclusivity extensions.

In the first scenario, under S. 666, a patent on a brand product has expired. When the generic company files its application with FDA for this product, which is no longer has patent protection, it must certify that the patent has expired. This certification will trigger a five-year exclusivity extension. Brand companies will be able to resurrect exclusivity on drugs no longer under patent protection.

Under the second scenario, the filing of an application for a generic version of a brand product with a certification that provides that the generic company is waiting to market its product until after patent expiry results in a five year exclusivity extension for the brand product. In other words, this filing, part of the current generic application process and required by federal law, automatically triggers additional five years of exclusivity under S. 666.

Unless these penalties are removed from S. 666, the effort by Congress to strengthen our nation's responsiveness to bioterrorism will in effect create a mechanism that resurrects exclusivity or extends patents. We will, in the name of preparedness, have dismantled any opportunity to continue to provide American consumers with drugs they can afford in a timely manner.

B. Wild Card Exclusivity

The second negative provision of S. 666 is the so-called ***wild card exclusivity***. Under this provision, a brand name manufacturer that conducts research on a possible biomedical countermeasure—or acquires such research more than one year before certification — receives an incentive of two years of additional market exclusivity on *any* drug it chooses. There are two significant problems with this provision. First, the bill offers no benchmark on the dollar magnitude of the investment in research or acquisition of research. A de minimis investment in research could buy a brand company billions of dollars in unearned revenue on any of its blockbuster drug products.

Second, this "wild card" exclusivity adds significant uncertainty regarding access to affordable medicines for our nation's healthcare system. An example makes this clear. Patent 1 for blockbuster drug L is scheduled to expire in two years and the product itself is not eligible for any patent extensions or marketing exclusivity. In preparation for the patent expiry, generic companies invest in the research, development, FDA approval and production of generic versions of Product L. They receive FDA approval and are prepared to launch generic product L upon the patent's expiration. Two weeks prior to launch, the innovator applies its "wild card," gained as a result of perhaps a minimal investment in development of a countermeasure on a totally different product. Consumers,

government, and private insurers will unexpectedly and unnecessarily have to continue to pay high monopoly prices for the expensive, brand name product, which has no relation to bioterrorism protection.

This wild card exclusivity represents the worst sort of cross-subsidy, essentially taking money from those who must pay for the drug, in the form of higher out-of-pocket costs, higher copayments, increased health insurance premiums or higher costs to government purchasers. This provision hurts all Americans with little benefit to national safety. Thus, the wild card concept must be removed, because it creates an unbalanced incentive for insubstantial investments in counterterrorism measures. If we do not remove this wild card from S. 666, we will be giving a blank check to brand phrma payable against the American public.

C. Extended Market Exclusivity

The third negative provision of S. 666 increases brand product market exclusivity in three instances for most of today's commercially marketed drug products. One component of this provision would increase ***the period of market exclusivity*** from five to 10 years for any new molecular entity with as little as one identified use as a biomedical countermeasure. The second component grants an additional 7 years of market exclusivity (up to 10 years) for a new use or dosage form of an existing marketed drug that can be used as a broad countermeasure agent. Further, it extends orphan drug exclusivity for broad countermeasures from 7 to 10 years. Finally, this component of S.666 extends the period during which generic manufacturers would be prevented from filing abbreviated drug applications from 4 to 9 years after the period of market exclusivity began. It is important to understand that market exclusivity is independent of the term of a drug's patent. These extensions of market exclusivity could thus work to lengthen the period of monopolistic pricing by these brand drugs and obstruct the entry of lower cost generics into the market for longer periods.

While it may seem ridiculous, the case can be made that any product could be granted additional exclusivity for something as simple as the conversion from a tablet to capsule dosage form, or liquid to solid dosage form. Or, if it could be shown that chemicals widely used, such as Zoloft® for depression, Plavix® for hear attacks, Effex® for anxiety, and Imitrex® for migraines, could play a role in treating the symptoms of a bioterrorism attack, additional exclusivity would be automatic under S. 666.

D. Patent Extensions

Fourth and finally, S. 666 provides ***open-ended patent extensions for broadly defined countermeasure agents for the full period of regulatory review***, which is defined as the time from when the patent is issued to the date of FDA product approval. As drafted, the bill sets no limitations on the number of years for such patent extensions, nor are there any limitations on the number of patent extensions per product. In extreme cases, this provision could be used for drugs that have long been off patent but for which their use as a bioterrorism countermeasure has subsequently been identified. In such cases, these

provisions of S. 666 could be used to reinstate patents for drugs, forcing generic alternatives off the market for unlimited number of years – which would equal the time in which the Patent and Trademark Office (PTO) granted the patent until the time FDA approved a countermeasure use. This provision also duplicates patent extensions already granted by PTO to compensate for time spent in PTO review, effectively giving brand manufacturers "double indemnity." Lastly, extended monopolies of currently marketed products can serve as a disincentive to brand companies to perform new research and development, including research and development on novel countermeasure agents. Again, as we always point out, competition – not indefinite product monopolies -- spurs innovation and presents a win-win situation for all.

In summary, the two provisions of S. 666 - the two penalties for generic manufacturers and the wild card exclusivity provision – that can harm consumers and delay access to more affordable generic medicines clearly have at best a tenuous linkage to the development and production of a novel countermeasure agent. The other two provisions—extensions of market exclusivity and patent extensions for the full period of regulatory review—are insufficiently defined under S. 666 and are so overly broad in that they apply to today's commercial marketed pharmaceuticals that they are ripe for widespread abuse.

Clearly, all four of these provisions would inflate drug prices, impose major obstacles to the entry of generic drugs into the market, and worsen the crisis faced by every American who must pay for all or a substantial portion of his or her prescription drugs, including millions of the uninsured and older Americans. They serve little sound purpose for strengthening BioShield I, and in fact, exact an exorbitant price from American consumers for no additional protection from terrorism. These provisions should once again be left on the cutting room floor as Congress recognized when it passed Bioshield I the first time.

IV. Appropriate Authority

GPhA believes that certain provisions of S. 666 have the potential to strengthen the research on, and development and production of novel countermeasure agents. However, we question whether establishing authority for these provisions within Homeland Security is wholly appropriate. We suggest that the Department of Health and Human Services, which already has direct authority over such important agencies as CDC, FDA, NIH, and the Public Health Service, may be better equipped to execute the objectives of BioShield I and extension thereto.

Similar to Bioshield I, S. 666 directs the Secretary of Homeland Security to develop a list of biological, chemical, and radiological agents that can be used as weapons of mass destruction and against which the development of new countermeasures is in the national security interest. Yet, the bill defines countermeasure agent as any drug product to treat, diagnose or prevent illness or conditions that are caused by being exposed to 55 overly broad possible target agents. Some of the identified agents are so ubiquitous that they are

responsible for common infections found in tens of thousands of patients across this country each year, such as E.coli, Salmonella, etc. The bill needs substantial refinement if we are to adequately prepare this country for a potential bioterrorism event; rather, than providing a substantial windfall to the special interest of brand pharmaceutical companies. Again, Bioshield I sets forth sufficient criteria to establish what are novel countermeasure agents and the means of researching, developing, manufacturing and procuring novel countermeasure agents, as well as needed diagnostic and environmental detection and warning systems.

Moreover, HHS, not Homeland Security, is the agency designated under Bioshield I to oversee this worthy and vitally important program. Certainly, more of the needed expertise and experience for developing countermeasures would seem to reside in HHS. We believe that the development of an appropriate definition of bioterrorism threats, and appropriate countermeasures, is a scientific one. We believe that the expertise to answer these questions, and develop an appropriate list of applicable countermeasures is unique to the Department of HHS and its agencies. Not placing this authority in the realm of science invites special interests to potentially "game the system" at the expense of Americans. We would propose that the responsibility for aligning America's brand and generic pharmaceutical industries to potential bioterrorism needs should remain with HHS.

V. Future Role of Generic Biologics

As an ancillary issue, we note with interest the provisions of S. 666 related to expansion of the nation's capacity to produce biologics. S. 666 directs the Secretary of Homeland Security to conduct surveys of biologics manufacturing facilities and to determine whether additional facilities are needed. It also charges the Secretary with determining whether technical advances might boost the nation's biologics output capacity and lower the costs of biologics. In addition, the bill establishes a biologics manufacturing investment credit, and would even preempt state and local zoning laws to facilitate the location of biologics manufacturing facilities.

GPhA shares the sponsors' concern about the nation's biologics manufacturing capacity and the costs of biologics. GPhA firmly believes that the time has come for the nation to actively explore ways in which generic firms might enter the biopharmaceutical field with similar price reductions to those which have accompanied the introduction of generic drugs. As Senator Hatch and members of the Judiciary Committee will recall, they held a hearing in June on the topic of "The Law of Biologic Medicine." Only last month, FDA held a public forum to discuss the science supporting generic biopharmaceuticals. Aggressively pursuing the creation of a regulatory process for generic biologics will address issues of manufacturing capacity and cost.

GPhA believes that our members have the scientific, development and manufacturing expertise necessary assure the nation of a supply of affordable generic biologics to address the need for countermeasures against agents used by terrorists.

VI. Summary

GPhA and its member companies strongly support the common overarching goal of both Bioshield I and S. 666, namely: to ensure that America has an adequate supply of drugs and other products that would serve as countermeasures to attacks by terrorists using biological, chemical, or nuclear weapons.

Specifically, GPhA strongly supports exploring the concept of extending Bioshield I to include three features of S. 666: (1) reducing product liability exposure of pharmaceutical manufacturers, (2) providing additional incentives in the form of tax credits and public funding, and (3) "fast tracking" the approval by FDA of countermeasure drugs and other agents. GPhA also supports additional funding for federal countermeasure research for novel drugs, vaccines, diagnostic tools and environmental detection devices.

GPhA, however, has grave concerns about four provisions of S. 666 that extend current patents, offer wild card exclusivity, penalize new generic drug development, and create unearned and unnecessary market exclusivity. These four provisions are extremely threatening to the economic viability of our nation's health care system.

GPhA respectfully urges the joint committees, as Congress did the first time around, to drop these four anti-consumer, anti-competitive provisions from the debate relating to extension of Bioshield I.

The responsibility of the Congress to protect American consumers extends beyond ensuring countermeasures for bioterrorism. It also includes ensuring that bioterrorism does not become the mechanism for economic disaster that rescinds the billions of dollars in savings this industry has created for American consumers. We must keep America safe from threat. But we must also ensure we do not threaten the health of consumers by placing life-saving prescription drugs once again out of their economic reach.

Thank you.

STATEMENT OF SENATOR EDWARD M. KENNEDY

HEARING ON BIOSHIELD II

OCTOBER 6, 2004

Joint hearings by Senate committees usually mean issues of special importance, and no issue today is more important than protecting the nation from terrorist attacks using deadly biological, chemical or nuclear weapons. I commend our distinguished chairmen, Senator Hatch and Senator Gregg, for holding today's hearing on this important issue. I also welcome our distinguished colleague, Senator Lieberman. I commend him for his interest in this issue, and for his leadership on the pending legislation to implement the recommendations for intelligence reform in the 9/11 Report.

We're obviously vulnerable to attacks with weapons of mass destruction, and our focus today is on strengthening our protections against biological attacks. We took a significant step in July to add greater protection by enacting the bipartisan legislation called BioShield, but additional action is essential. I'm hopeful we can work together to enact a "BioShield II" bill to encourage the biotechnology industry and the pharmaceutical industry to develop the biodefense measures we urgently need to protect our security.

[illegible]

Incentives to industry are an indispensable part of our defenses against bioterrorism, but the incentives have to be appropriate. We can't afford to squander resources on needless

giveaways. Some want to reward companies that develop countermeasures by granting greater patent protection – not for new drugs against anthrax or Ebola, but for current blockbusters in other areas. In return for developing a new vaccine against a deadly virus, a company would expect a patent extension on another drug worth billions of dollars in sales of unrelated products.

[MV: Add chart showing value of patent extension for best selling drugs]

If these "wildcard" patent extensions are given to the 9 highest selling drugs, for example, the cost to consumers would be over $30 billion. That's equal to a whole new NIH every year, as a gift to the drug industry.

Already, millions of Americans have to make impossible choices between paying the rent, or putting food on the table, or purchasing the drug they need. Many of us support responsible bipartisan proposals to make prescription drugs more affordable by allowing imports from Canada and other countries or allowing Medicare to negotiate discounts for the nation's seniors. Making prescriptions even more expensive would be a giant step in the wrong direction.

In developing new legislation to build on the success of BioShield, it may well make sense for the federal government to contract directly with private sector firms so that the vaccines and drugs can be developed as rapidly as possible.

This approach has already been used successfully on one high priority aspect of the issue. Secretary Thompson used it to obtain additional quantities of smallpox vaccine. He contracted

with Acambis, a biotech company in Massachusetts, to produce enough vaccine for the national stockpile to treat every American. In addition, Acambis will also produce, test and deliver up to 2.5 million doses of a new generation of the vaccine. The cost of these contracts is $140 million.

At the same time, NIH scientists conducted research to determine whether existing stocks of the vaccine could be diluted to treat more people, if necessary. The cost of this research was $34 million. If a drug firm had done the same work under a transferable patent extension of the kind being proposed by some, the cost to consumers could have been in the billions of dollars.

[illegible]

Obviously, the approach used for smallpox makes far more sense than giving a subsidy worth billions of dollars to drug companies to get the same results.

A related issue is fair compensation for persons who have been injured by faulty products. The Administration's misguided smallpox vaccination program granted liability protection for manufacturers without adequate compensation for patients. As a result, health care workers stayed away in droves from the vaccination program. We also need to make sure that any indemnity for manufacturers is not excessive. We must also see that health care workers receive the training and workplace safety protections needed to safeguard their health.

After a long battle in Congress on the smallpox issue, we finally established a reasonable compensation program, but the damage had been done. Of the ~~500,000~~ 10 million people who ~~should have~~ were intended to

receive the vaccine
~~been vaccinated~~ under the smallpox preparedness program, only 40,000 have received the
less than 1 percent
vaccine so far -- ~~8 percent~~. Obviously, we can do better.

In addition to developing new antibiotics, we should consider measures to enhance the effectiveness of those already on the market. We must stop squandering the effectiveness of medically important antibiotics by using them indiscriminately in agriculture. I have introduced legislation with Senator Snowe to end this abuse, and this measure should be part of our strategy for BioShield II.

Controls on dangerous pathogens are essential to prevent dangerous biological materials from falling into the hands of those who would do us harm. In the bipartisan legislation on bioterrorism enacted two years ago, Congress included such controls. Since then, leaders in medical research have offered recommendations on improving the safeguards to allow greater flexibility in their implementation, while still preventing the materials from falling into the wrong hands.

In some cases, productive collaborations with scientists from other nations are impeded by the lengthy delays they face in obtaining visas for legitimate work or study in America. GAO and others have recommended improvements in visa procedures, so that international scientific cooperation is not hindered by unnecessary administrative delays.

I look forward to working with my colleagues to resolve these issues and develop the BioShield II proposal. I join in welcoming Dr. Bartlett from Johns Hopkins, whose leadership in

the medical community has been so influential in enhancing the nation's preparedness for bioterrorism. I look forward to the testimony of our other witnesses and Senator Lieberman and to expediting action to strengthen our protection on this basic part of our homeland security.

Testimony of

Jeffrey P. Kushan
Partner
Sidley Austin Brown and Wood, LLP

Before the
Committee on Health, Education, Labor, & Pensions
and
Committee on the Judiciary
United States Senate

Hearing on
Bioshield II: Responding to An Ever-Changing Threat

Chairman Hatch and Chairman Gregg, and distinguished Members of the Committees.

Thank you for providing me with the opportunity of testifying before you today on the issue of market incentives for encouraging development of countermeasures to respond to bioterrorism threats. I am testifying in my personal capacity, and the opinions I offer in this testimony are my own.

In my testimony, I will address the issue of intellectual property incentives that have been proposed for inclusion in BioShield II. In particular, I will be directing my testimony toward the questions of patent term restoration, a patent bonus concept, and data exclusivity proposals.

Earlier this year, the Congress started an important process of creating economic and other incentives to encourage industry to discover and develop new drugs and other technologies to respond to the threat of bioterror agents. It did this by setting up assured procurement opportunities, expedited and relaxed drug evaluation procedures, and other measures. Project Bioshield I is a well-designed effort and has enhanced incentives for the public and private sector to conduct research and development related to this important field of endeavor.

As many of the witnesses who testified on the original Bioshield legislation observed, the provision of an assured Federal Government purchasing authority and assured funding for research and development will only go so far in encouraging the development of new products. Additional measures are needed to encourage creation of an industry that will commit its own funding and take the risks necessary to bring innovative new products to market. And, as was previously observed, to be viable, the biodefense industry – and the markets from which it will obtain its capital – must view the opportunities in this field to be comparable to those in other fields of pharmaceutical industry. Thus, the environment in which this industry will exist must have the same type of market incentives and certainties that exist in the biotechnology and pharmaceutical industry today.

A. Metrics for Success for a Biodefense Industry

A viable biodefense industry is one that engages in new product discovery and development motivated by the opportunity for market success, rather than through government support or indirect subsidies, standing alone. The factors that will be necessary for such an industry to evolve in the United States are the same as those that have proven necessary for our successful U.S. biopharmaceutical research and development environment. These factors can be summarized briefly as follows.

1. Assured Market Exclusivity for Successful Products

The biotechnology and pharmaceutical industries are extremely market-savvy, and the market is extremely savvy about these industries. What this means is that the market immediately rewards – and also severely punishes – those companies that stray from an essential formula for success. That formula requires the new venture to demonstrate not only that it has created an innovative new product or service, but that it will enjoy meaningful and assured market exclusivity for that new product or service.

Meaningful market exclusivity in these industries means that the innovator will face only technology competition, not price competition for a reasonable period after its product launches. In other words, the market assumes that the primary risk (if any) of competition during the market exclusivity period will come from *different* products that must be independently shown to be safe and effective ("technology" competition), and not from significantly lower cost copies of the *same* product ("price" competition). The consequences of earlier price competition are obvious – the sooner that price competition arrives, the smaller the overall return will be for the innovator and the investors that backed that innovator. And, of course, the smaller the possible return, the weaker the incentive will be to undertake the venture and fund it. In simple terms, unless companies can show that they have a decent chance of making a significant return on an investment, they will lose the fierce competition for capital.

Companies must also be able to convince savvy and skeptical investors that their market exclusivity will be relatively certain. In my experience, most companies and ventures tolerate a fair amount of risk of competition from other innovation in the biopharma field. This is in part because of the high failure rate in this industry, and in part the broad diversity in possible new products that can come out of basic research and development activities. Thus, while many examples exist where an innovator has faced competition from another innovative product within a year or two of the first product's market launch, it is more common that several years will pass after the first of a new class of products has been launched. Obviously, the longer the period of market exclusivity, the stronger the incentive for investing in research and development of new products. But, within the decision-making process of funding research and development toward a commercial product, this risk is accepted as a legitimate one that can be managed.

What is not tolerated by the investment community is risk that is unpredictable. For example, the prospect of political interventions in the market that operate to deprive a

company of its market exclusivity after that company has finally brought a product to market can be devastating to the industry. Similarly, a legal system that offers uncertain market exclusivity is very difficult to use to assure skeptical investors. Uncertainty in this respect means that a company that does the work to qualify for market exclusivity – either through patents, data or other market exclusivity – either is not granted that exclusivity, or is granted less exclusivity than anticipated.

2. Efficient Technology Transfer and Rights that Protect the Entire Venture

There is a diverse community of entities that contribute to the discovery and successful development of new pharmaceutical products. The members of this community include the public research community, including NIH and the university sector, small startup entities, the capital markets, and, critically, larger biotechnology and pharmaceutical companies. A close relationship among these entities is essential for the biotech and pharmaceutical – and correspondingly a future biodefense industry –to exist and succeed, and for new ideas to move from the lab bench to the market.

Of course, a continuing U.S. success story is the close partnership between the public sector research community and the commercially-focused biotechnology and pharmaceutical industries. This partnership has effectively moved scientific discoveries and advances from the lab into the stream of commerce. Each sector has its role to play in this partnership. The public research sector plays the critically important role in advancing basic science, and in identifying new drug candidates or platforms for drug discovery. The primary role of the private sector is the difficult task of translating advances in science into new products and services, and in taking the steps needed to bring these products to market.

The promise of market exclusivity that protects all members of the development venture is the glue that holds this environment together. Often, a compound discovered in the university lab becomes the basis of the ultimate product. Just as often, this is not the case, but the early work plays a significant role in identifying and developing the final product or service that does reach the market. Either way, the early patents that are awarded on these innovations – frequently to university researchers or small startup companies – become the patents that are relied upon to protect the products that eventually reach the market.

Efficient and effective technology transfer, through the Bayh-Dole Act and other mechanisms, is thus essential. Effective technology transfer means that the early stage developer can transfer intellectual property rights it has obtained that will protect its efforts, along with the work of a commercially-focused partner, and ultimately will enable the commercial partner to achieve market exclusivity in products that actually reach the market. Thus, efficient technology transfer enables a company to take in a promising candidate and begin the difficult process of developing these candidates into actual products and services.

In recent years, there has been a trend toward more partnerships between young biotechnology companies and established biotechnology or pharmaceutical manufacturers. Fewer and fewer companies are taking the highest risk path that starts with drug discovery and ends with the launch of a product. Instead, many biotech companies focus on early stage drug identification and development. Once the small biotech company has identified a promising lead, confirmed its potential and has secured strong intellectual property rights around it, it then seeks to partner with a larger entity to take the lead in clinical development, manufacturing and marketing of the product. These partnerships efficiently leverage the ability of the small biotech company to efficiently conduct focused discovery and characterization work, up to the phase of pre-clinical animal investigations, or perhaps small scale human clinical investigations. The larger entity then takes on the more challenging, expensive and riskier phases of product development; namely, human clinical investigations, development of manufacturing process technology to scale up production to meet expected product demands, drug approval, product launch, domestic market development and foreign approval and marketing.

In recent years, the established pharmaceutical and biotechnology companies have also played a more prominent role in financing the development of these companies and products. Thus, while the early stage biotech company continues to depend primarily on venture capital or other private sources of capital, there is an earlier intervention by established biotechnology or pharmaceutical companies in the development of these companies and their products.

3. Effective and Assured Market Exclusivity is Essential

As noted above, the "glue" that holds these efforts together is the assurance of market exclusivity. There are several mechanisms by which market exclusivity is granted to pioneer drug developers, including patents, data exclusivity (along with pediatric exclusivity) and orphan drug protection.

(a) Patent Exclusivity

Patents give their owner the right to exclude others from making, using, selling, offering for sale or importing the patented technology for a specific period of time. Thus, the patent theoretically can be used to prevent competition in the sale of the products that are covered by the patent.

Importantly, patents do not "automatically" confer market exclusivity. Instead, they have to be enforced by the patent owner against the infringer through litigation in the Federal district courts. Patent litigation is notoriously unpredictable, risky and expensive. Moreover, given the fact that the most patents are sought many years before the identity of a final product is known, there are substantial risks that these early patents do not effectively cover the final product that is being marketed. And, because a patent can be properly granted only for inventions that have not been publicly disclosed, it is often only the innovators at the very beginning of the drug development process that can obtain

patents that will cover the commercial product. Thus, universities, public research organizations and small start-up biotechnology companies often own the patents that cover the ultimate product, rather than the company that has done the clinical work and product development necessary to bring the product to market.

Certainly, one benefit of the U.S. environment is the Hatch-Waxman Act. This Act provides a way for pioneer manufacturers and generic producers to resolve disputes over patents before the generic product has been launched. Under the Hatch-Waxman Act, the generic producer must provide detailed reasons as to why they believe a patent listed for the drug is invalid or would not be infringed. If the producer does so, the patent owner can commence an action for infringement. Before a final resolution of that infringement litigation, the generic application will not be approved by the FDA (subject of course, to a 30 month limit on such a stay of approval). Thus, under the Abbreviated New Drug Application procedure, the patent owner can intervene to prevent infringing products from entering the stream of commerce, and keep them from doing so until questions over the scope and validity of the patent are resolved.

(b) Data Exclusivity

The other primary form of market exclusivity for pharmaceuticals is data exclusivity. These rights give *de facto* market exclusivity for those companies that conduct the original clinical investigations of a drug to demonstrate the new drug is safe and effective. Companies that wish to market generic copies of a product without performing their own independent clinical investigations to prove the drug is safe and effective must wait for a certain number of years after the first or "pioneer" drug product has been approved. Under the U.S. system, five years of data exclusivity are provided for drug products containing an active ingredient that has not been previously approved, but only three years are provided for new indications or supplements to previously approved drug products.

(c) Pediatric Exclusivity

Companies that demonstrate that their drug product is safe and effective through clinical investigations in pediatric populations can obtain an additional six months of exclusivity for doing that clinical work. The pediatric exclusivity provisions have been an effective incentive for companies to undertake this work, which often results in very small populations of patients that benefit from the clinical work. Pediatric clinical investigations are very difficult to conduct, and the absence of significant pediatric patent populations ordinarily is a strong deterrent to seeking authorization to market products to pediatric patients.

(d) Orphan Drug Exclusivity

Orphan drug exclusivity is another form of market exclusivity mechanism for new drugs. Orphan drugs are those drugs that have limited patient populations (e.g., less than 200,000 with the particular indication). A company that demonstrates the safety and

effectiveness of a new product to treat an orphan indication is given seven years of exclusivity for that product and that indication. Orphan drug exclusivity is broader in effect than data exclusivity; other versions of the same drugs for the same indication may not be approved for marketing prior to the expiration of seven years from the approval of the orphan drug. Thus, unlike data exclusivity, orphan drug exclusivity blocks approval of both generic versions (e.g., copies of the drug that do not include clinical data) as well as other drugs that are supported by independent clinical evidence of safety and effectiveness.

Each of these mechanisms for market exclusivity has played an important role in stimulating industry to develop and bring to market new drug products. The guarantee of market exclusivity has encouraged companies to pursue development of new products despite significant risk of failure, offer a significant return on investment. Special market exclusivity incentives – such as orphan drug or pediatric exclusivity -- have also proven to be very effective in overcoming economic obstacles that have deterred drug development efforts in these settings. For example, few orphan drugs were developed prior to enactment of the Orphan Drug Act. The reason is simple; drugs that have a very limited patient population inherently have a very limited capacity to turn a profit, much less a strong profit. The orphan drug authority changed this economic equation, and has stimulated the development of more than 250 approvals for orphan indications. Similarly, pediatric exclusivity has proven to be an effective economic incentive for companies to take on the task of proving their drugs are safe and effective in pediatric populations. This indirect but strong incentive of an additional six months of market exclusivity has encouraged companies to take on this challenging task of conducting pediatric clinical investigations, with over 100 pediatric approvals since the legislation was enacted in 1998.

B. Market Incentives for Research and Development of Countermeasures for Bioterror Pathogens

As noted above, the Congress has created special market exclusivity mechanisms to encourage the private sector to develop new drugs in setting where ordinary market incentives have proven to not be effective. These special market exclusivity measures have been effective in stimulating the development of new products for orphan indications and for pediatric clinical investigations.

As in the case of orphan drugs and pediatric indications, the market does not provide a clear incentive for companies to develop countermeasures. The significant reasons for this can be summarized as follows:

- *There is no assured or consistent market for these products.* While there certainly will be products that have "dual use" capabilities, the non-countermeasure applications of these products are not assured. Moreover, the goal is to develop innovative new products that can respond to a variety of unknown challenges. It is unlikely that "off the shelf" products will meet these needs

- *When a need arises for countermeasures, there could be severe demands for the volume of products.* Depending on the scale of the need, immense stress could be placed on the ability of a manufacturer to make products available in sufficient quantities. This stress may cause the manufacturer to turn to other producers to meet product demand. Alternatively, it may cause the manufacturer to maintain artificially large stocks of products, despite the absence of market demand for those products.

- *The primary purchaser is likely to be the Federal Government in an emergency setting.* The private sector and capital markets remember the reaction of the Federal Government in response to the anthrax scare in 2002. The pressure put on the manufacturer of Cipro® to slash prices – primarily the implicit threat of procuring the drug from an alternate supplier – sent a clear message to the private sector that there is no guarantee of a market driven price for these types of products.

Certainly, Congress has taken an important step in addressing these problems through BioShield I. These steps have led a number of companies to initiate work on development of countermeasures for bioterror pathogens. However, this incentive structure is limited in its scope and power to induce the private sector to start development efforts for these types of products. Thus, to complement these efforts, more direct and powerful market incentives are needed to overcome these significant deterrents for industry. The provisions of the Lieberman-Hatch proposals (S.666) appear to be well-designed to address these market challenges.

1. Full Patent Term Extension Authority

An important part of the Hatch-Waxman Act is its authority for a patent owner to extend the term of a patent to compensate for periods of time while a drug is in the regulatory review process. Under 35 U.S.C. §156, however, several limits are placed on the duration and nature of the extension. For example, the patent during its "extended" period can only be enforced against drugs the same drug product (within certain limits). The effective period of the patent (i.e., the period from the date the drug is approved until the patent expires) cannot exceed 14 years, and any individual extension cannot exceed five years. The way the present extension is calculated also gives only partial credit for phase I and II clinical investigations.

Section 5(c)(1) of Lieberman-Hatch would create a patent term extension authority that is not subject to these arguably arbitrary limits. Unlike present §156, the period of extension that will be available corresponds to the full period of regulatory review – including phase I activities –and is not capped by the 14 year effective term and 5 year individual extension limitations. This is important, as it may be possible to get a countermeasure approved on a faster track than the ordinary path a pharmaceutical product. In the absence of this new basis for calculating the extension authority, an otherwise deserving countermeasure patent might not qualify for a meaningful patent term adjustment.

2. Patent Bonus

An innovative feature of Lieberman-Hatch is its "patent bonus" provision. We note that there are many design options possible for creating such a bonus system. Under §5(d)(1), an entity that develops a countermeasure will be given the right to extend the term of one patent it owns, regardless of whether the product is the countermeasure.

The patent bonus appears to be limited in several key respects.

- Only an unexpired patent can be extended; it cannot operate to take revive expired patents or take generic products off the market.

- The patent bonus is only awarded once the company has successfully developed its new countermeasure, and fully met all procurement requirements and Government-specified product needs.

- A company that attempts to develop a countermeasure and ultimately fails will not get a patent bonus.

- Measures are included that prohibit marketing of a patent bonus – including the prohibition against acquisition for the purpose solely of obtaining the patent bonus and patent ownership requirements. These measures will effectively prevent improper use of the patent bonus.

- The only entities that appear capable of benefiting from the bonus are small businesses with less than $750M in revenue.

- The patent that is to benefit from the bonus authority must have been issued before the countermeasure marketing authority was granted.

These measures, along with other aspects of the legislation will ensure that the patent bonus is not abused.

The patent bonus appears to be an indirect but powerful incentive for companies to undertake countermeasure development notwithstanding the lack of commercial potential of such products. It is analogous to the pediatric extension authority, in that it awards an extension of market exclusivity for any indication for the drug product, in exchange for the sponsor successfully undertaking development of the countermeasure. To be successful, the patent bonus must (i) be assured, and (ii) encourage companies to shift existing resources to develop new countermeasures. An obligation that seeks to require a company to devote profits from products that have been given a patent bonus will not induce the pre-development activities that this patent bonus is designed to do. Moreover, the more "strings" that are attached to the patent bonus – particularly with how those strings limit future research and development activities of the company – the less effective the patent incentive will be. The experience of industry is that funding and

incentives that come with strings attached that limit the commercial discretion of companies typically fail to win the confidence of companies and their investors.

3. Extended Data Exclusivity and Orphan Drug Exclusivity Periods

The third incentive in Lieberman-Hatch is an extension of data and orphan drug exclusivity periods for new countermeasures.

The legislation would extend the duration of new chemical entity (NCE) countermeasures and new indications/supplements/etc from the 5 and 3 year periods up to a 10 year period. Patent challenges that now are possible in the 4th year from product approval for NCE drugs and at any time after approval for non-NCE drugs may be made at nine years from product approval. Also, if the countermeasure qualifies as an orphan drug candidate, it also can obtain up to ten years (instead of seven) of orphan drug exclusivity.

The extended data exclusivity and orphan drug act periods are justified given the lack of certainty in when these countermeasure products might be needed. A data exclusivity period that pushes out the expiration of data exclusivity protection will be far more valuable to the industry than the 3 or 5 year options available (and which might expire before the commercial product actual is put on the market).

C. Conclusions

Product development against known diseases and disorders is immensely challenging and unpredictable. The industries that have undertaken the business of finding new products to treat these known diseases do so based on the availability of strong market exclusivity protections for their products. They understand that market demand for their products, coupled with strong market exclusivity through patents, data protection and other measures creates the possibility of a high return on investment. The incentives plainly work – experiences from the Orphan Drug Act and pediatric exclusivity show that strong economic incentives can effectively overcome market-based impediments to product development.

By contrast, the threats of future bioterrorism are unknown and cannot be easily predicted. Even more pronounced market exclusivity measures will be necessary to encourage the private sector to enter and stay in this market, and to successfully develop countermeasures. The measures outlined in Lieberman-Hatch seem well-designed to achieve the goal of having companies stay active in the biodefense industry so that they can respond quickly when new threats materialize.

Thank you for your time and consideration of my views.

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November 12, 2004

The Honorable Senator Orrin G. Hatch
Chairman
Senate Judiciary Committee
224 Dirksen Senate Office Building
Washington, D.C. 20510

ATTN: Barr Huefner

Dear Senator Hatch:

I wish to thank you and Senator Gregg, and the Members of the Committees on the Judiciary and on Health, Education, Labor and Pensions, for giving me an opportunity to provide my personal views on the intellectual property provisions of S.666 (Bioshield II).

As I indicated in my testimony and in the hearing, I was asked to testify in my personal capacity on certain provisions of the Bioshield II legislation. I am a practicing patent lawyer, and work with a wide variety of patent-dependent companies, particularly those in the biotechnology, pharmaceutical, and software industries. I drew from my experiences as a patent lawyer in preparing and delivering my testimony to the Committees. In particular, I sought in my testimony to explain to the Committees my view that the measures that were included in Bioshield I are positive, but, standing alone, would be unlikely to cause the private sector to shift resources (financial and otherwise) to conduct research and development to identify and bring to market new countermeasures to biological terror agents. I also indicated my belief that the existing commercial development environment for biotechnology and pharmaceutical products, including as established by the Bioshield I legislation, does not provide a significant stimulus for companies to engage in such research and development efforts.

Let me again stress that my testimony then and the answers I am providing through this communication are my personal opinions. During the hearing and in some press contacts I have had since the hearing, it has been suggested that the views I offered were on behalf of a client. This is not the case. My views, expressed then and now, are my own. They are based on my experiences in working with small and large companies trying to develop new products and from working with venture capital funds and other entities that are partnering with these companies. I

also base my views on my experiences inside and out of the United States government, where I had the opportunity of working on legislation and other sources of patent policy.

At the hearing, I testified that the market incentives that exist today generally do not induce biotechnology or pharmaceutical companies to undertake development of countermeasures. I observed that some progress has been made through the assured procurement authority of Bioshield I. However, I also observed that competition is fierce for limited sources of private capital to invest in research and development of new biotech and pharmaceutical products. For example, I noted that countermeasures, once developed, may never be purchased, or may be purchased on terms that do not provide a strong economic reward for the developer of the countermeasure. I believe that is the reality of the market today, and that unless other mechanisms are created, limited market demand will cause few companies to invest in development of countermeasures – particularly at the expense of development of other types of healthcare products.

Your letter presents two questions from Senator Kennedy. The first question is:

> You say that wildcard patent extensions are analogous to the system of rewarding drugs for pediatric indications with six months of extra exclusivity. Isn't it the case that the pediatric exclusivity applies only to the drug that is being developed for children – not to whatever blockbuster drug the company selects?

In my testimony, I indicated that the patent bonus concept was analogous to the system of pediatric extensions for pharmaceutical products. The basis for my opinion was that pediatric exclusivity – like the patent incentive for countermeasures for bioterror agents – creates a *general* economic incentive that is *not proportional* to the actual market opportunity associated with the *pediatric* sales of the product. Except in rare cases, the pediatric population for a drug product will be a small, and often tiny, fraction of the overall market for the drug. Revenue from sales to this small fraction of the market will be limited – meaning that there is not much of an economic incentive for a company to do the clinical testing of the drug necessary to permit pediatric sales, given the significant cost and difficulty of doing such testing. In return, however, a pediatric extension provides the pioneer manufacturer with six additional months of *general* market exclusivity, during which only that manufacturer can sell the product. The pediatric market exclusivity thus does not give rights only with respect to sales to the pediatric segment of the market for the drug. Instead, it gives the pioneer manufacturer an economic benefit from exclusive sales to the entire market.

I testified that this system has worked well – meaning that the economic incentive of additional six month period of exclusive sales of the product has stimulated a significant amount of research and clinical development of pediatric versions of drug products. Since inception of the provision, over 100 drugs have been approved for pediatric indications. In my view, this success is perfectly in line with the Congressional intent of providing the additional six month exclusivity period (i.e., Congress wanted pioneer drug manufactures to develop and bring to market versions of approved drugs suitable for use in pediatric patients, and this has happened with great success).

As is the case for pediatric exclusivity, the patent bonus provisions in Bioshield II seek to provide a *general* economic incentive for companies to develop and bring to market new drugs that can be used as countermeasures. Also as is the case for pediatric drugs, the current market incentives for a company to develop a new countermeasure are insufficient. In my testimony, I observed that there may never be any sales of a product developed as a countermeasure. At a minimum, the market demand for such a drug will be extremely uncertain, both as to whether there will be any significant sales of the product, and certainly as to the profit potential of such a drug. And, as I observed at the hearing, any actual sales of the product may not arise until *after* the test data exclusivity period provided by the Hatch-Waxman act has expired -- meaning that this incentive (i.e., market exclusivity for 3 or 5 years after approval) may never yield any commercial benefit for these drugs, because the drugs will not be sold during this limited period after approval.

For the above reasons, I indicated that the creation of a patent bonus provision, such as that outlined in Bioshield II, would, like pediatric exclusivity, create a *general* economic incentive for the private sector to take the risks of investing in, conducting research and development, and bringing new countermeasures to market. Such a market incentive would be clearly understood and definite, and would not be limited to actual sales of the countermeasure, which may be non-existent or on non-commercially viable terms. Thus, I continue to believe the two regimes would be analogous.

The second part of the question asks whether the pediatric extension only applies to a specific, previously approved drug that is evaluated for pediatric approval. The answer is yes. As I tried to explain in the hearing, the pediatric extension solution was a response to the specific problem of an inadequate market incentive for companies to test their products for use in pediatric populations. The market, in simple terms, did not provide an economic incentive sufficient to encourage companies to undertake this difficult task. This is precisely the situation facing companies contemplating development of new countermeasures – an insufficient market incentive to undertake the risky effort of developing a new countermeasure. And, the fact that the pediatric exclusivity bonus is linked to a specific drug does not detract from the analogy. Instead, it addressed the precise problem Congress identified – the encouragement of research and development to support approval of a previously approved drug for use in pediatric patient.

I note that the motivation for this question may be a concern over how the patent bonus is structured in the legislation. I sought in my testimony to indicate that I was addressing the *concept* of a patent bonus provision. It is my belief that creating a defined period of additional patent exclusivity for a drug that is actually being sold is a definite and understandable economic incentive. I would anticipate that the Congress would incorporate into such a provision measures it deemed appropriate to ensure that the measure operates only as intended (e.g., that it would not be possible to obtain multiple extensions of a single product).

The second question posed by Senator Kennedy is:

> It's extremely lucrative for a company to develop a new drug for baldness or obesity or depression. Do you think the incentives in any BioShield II legislation need to be just as high to get big drug companies to participate in biodefense? Will it take billion-dollar subsidies to get them to participate?

In my experience, the vast majority of companies that engage in biomedical research are focused on developing new and effective drugs for treating human diseases that either afflict large numbers of people, or are serious life-threatening illnesses. Contrary to the suggestion in the question, in my experience the primary diseases being investigated are cancer, heart disease, diabetes, Alzheimer's and a variety of communicable diseases. These companies are driven primarily by two factors; namely, the desire to find a solution for a significant unmet medical need, and the ability to deliver a good return on investment. It is an extremely challenging field, and one that provides immense benefits to American public – and indeed the world. Ask any cancer patient that has been given a new hope of being cured.

A significant public and private investment is needed to decipher the mechanisms of disease. But, the true challenge of developing a new drug is to identify how to exploit this scientific knowledge and develop an effective therapeutic intervention. Doing so not only requires innovation as to the design of the drug and intervention, but immense effort to determine how to, for example, manufacture the drug in sufficient quantities and test it to prove that it is safe and effective.

In my experience, those who invest in new drug development are fully aware of these variables. Whether they are early stage venture capital funds or established pharmaceutical or biotechnology companies looking to partner in the drug development process with a small startup company, the questions are the same; namely, (i) is the technology viable, (ii) what is the potential return on investment, and (iii) will the product enjoy an effective period of market exclusivity delivered by patents and test data protection?

Senator Kennedy's question frames the issue as being whether a countermeasure must have the market potential of a "blockbuster" drug. Certainly, a blockbuster pharmaceutical product sold to millions of Americans represents a huge economic incentive. Very few drugs, however, become blockbusters and I believe the premise of the question misplaces the actual focus of the investment decision on a new drug development effort.

In my opinion, the correct question is whether Congress can create a market incentive that makes countermeasure development compete effectively for limited private sector funds and resources. The issue is competition for limited research dollars, not subsidization. In other words, if a company knows that it will have a certain economic reward – an extended patent exclusivity period for a successful drug – then the risk it faces of unsuccessfully developing a new countermeasure, or of developing a drug that will never be sold, can be balanced against a defined market return (i.e., actual sales of a successful product). A definite and understandable market incentive for countermeasures development would make development of such countermeasures attractive to the private sector. Such incentives also would make the investment and development decisions facing a company comparable to those used to decide whether that company should pursue development of drugs for cancer, diabetes, heart disease and other major illnesses affecting the American public.

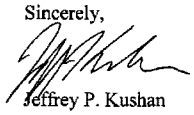
In the question, Senator Kennedy asks whether the market incentives for countermeasures drugs must be comparable to those for what I believe he intended to mean were huge blockbuster drugs. I am unable to put a strict numerical figure on a threshold incentive. Instead, in my view, the degree of potential market return will define the strength of the incentive. Thus, allowing a company to enjoy two additional years of market exclusivity for a drug that earns billions of

dollars of revenue each year will create a very strong incentive, and more countermeasures certainly will be developed in response to that strong incentive. Providing one additional year of exclusivity for any drug will create a smaller, but still discernable incentive. Limiting the patent bonus to drugs that have limited annual sales (e.g., <$100 million annually) will likely make a patent extension incentive ineffective. I note that drugs having only this scale of return are often not funded out of private capital because the risks associated with those drugs is excessive, particularly relative to the limited potential return. For example, one factor a funding entity considers is the scenario of the drug being able to enjoy only new drug exclusivity (i.e., because the drug may not be effectively covered by a patent, or may have its patent invalidated by a generic company after the data exclusivity period for the drug expires). The present environment of assured patent challenges means that most entities must use this "worst case" scenario of a five year period of sales for a new drug product, meaning that the developer of the drug must be able to not only recover the $350 to $750 million of costs of developing and launching the drug, but also deliver a return substantially in excess of those costs. I note that few commercially-focused entities would invest in a drug development venture if the only possibility were to simply recover the investment being made.

As I noted above, I do not believe it is possible to give a simple answer to the question of what the threshold of potential revenue of a countermeasure must be to encourage private entities to undertake developing such drugs, rather than other types of drugs. The best answer I can give is that the market incentive for developing new countermeasures must be strong and dependable enough to offset the negative factors regarding countermeasure development (e.g., limited or no sales of the product). The existing environment which provides only the incentives of assured purchases of countermeasures will induce only a handful of companies to undertake countermeasure development. To encourage companies to prioritize countermeasure development – to pursue development of those, rather than other drug products funded through private capital – requires a market opportunity that is far beyond the opportunities established by Bioshield I.

I hope the answers provided above are useful, and look forward to responding to any further questions the Committees may have.

Sincerely,



Jeffrey P. Kushan

cc: Senator Joseph Lieberman

Statement of Senator Patrick Leahy
"BioShield II: Responding to An Ever-Changing Threat"
Joint Hearing of the Senate Judiciary Committee
And the Senate Health, Education, Labor and Pensions Committee
October 6, 2004

Mr. Chairman, the focus of today's joint hearing with the Health, Education, Labor and Pensions Committee is an important one. In our increasingly uncertain world, the American people deserve assurance that government and industry are doing all that they can to protect their health and well-being. But this morning, the answer to that question is far from clear.

As we meet today to discuss how to prepare our nation for the dire possibility of a catastrophic bioterrorist attack, the likes of which I hope we will never see, we learn that we are not prepared to meet the biological threat that comes every year -- influenza.

I had hoped that the Bush Administration would have learned their lesson from last year's experience with flu vaccine shortages. Instead, we see health officials across the country, including in my home state of Vermont, asking healthy people to forgo their flu shot. I think the American people deserve an answer from the Bush Administration as to why it had not planned and prepared better. If they can not be prepared for the seasonal flu -- an annual occurrence -- what does that portend about their ability to prepare for biological terrorist attacks?

One of the primary problems with the flu vaccine that is highlighted by the Administration's inability to ensure sufficient supply appears to be the concentration of producers. This market concentration is something that the government can control. The brand pharmaceutical industry is too concentrated and they fiercely lobby to extend their patents to prevent generic pharmaceuticals from giving consumers more affordable medicine.

Our constituents and members of Congress need to ask why this country is so dependent on just two suppliers of this important vaccine. With all the pharmaceutical suppliers in this country, why is our government relying on a foreign supplier which has just been put out of business by the British government.

I would hope the big brand pharmaceutical companies would demonstrate their capability to respond to this crisis by answering the call of this flu vaccine problem rather than pushing for patent extensions and windfall profits. We must address the potential crisis

and make agreements to license and produce the vaccine the world needs now. We must not find ourselves in this position again.

I understand personally the pressing need to develop treatments for deadly biological, radiological and chemical agents that could potentially be used as instruments of terror – I was the target of an anthrax-laced letter in 2001. Although the strain of anthrax sent through the mail to me, Senator Daschle, and others could effectively be treated with existing antibiotics, effective countermeasures currently exist for very few of the most dangerous potential biological, radiological and chemical threats.

I am pleased that Congress took action this year to enact the Project BioShield Act of 2004. I commend Senator Kennedy for his leadership in that effort. Under that bill, Congress approved streamlined procedures for bioterrorism-related federal procurement, research funding, and hiring needs. We guaranteed that the federal government would purchase new countermeasures through an advance appropriation of $5.593 billion over the next 10 years and we established the authority for emergency use of as yet unapproved countermeasures. These are all common-sense incentives to provide for the development and delivery of new countermeasures to the American people.

Today we are examining the question whether further action on the part of Congress is needed to fulfill the original goals of Project BioShield, with a particular focus on legislation introduced last year by Chairman Hatch and Senator Lieberman. The Biological, Chemical, and Radiological Weapons Countermeasures Research Act of 2003 (S.666) proposes a vast list of intellectual property, antitrust, liability and tax giveaways to provide the pharmaceutical and biotechnology industries with further incentive for the development of new countermeasures.

I have serious concerns about the wide-ranging consequences of this bill. It strikes me as giving everything but the kitchen sink away to the brand pharmaceutical industry. Its sweeping scope threatens to dismantle the careful balance of intellectual property rights struck with the Hatch-Waxman Act, and to roll back the gains made in recent years to lift the barriers preventing affordable generic drugs from reaching the market under the Schumer-McCain Greater Access to Affordable Pharmaceuticals Act.

The definition of "countermeasure" under S. 666 is so broad as to likely affect the patent life and terms of market exclusivity on virtually all current and new pharmaceutical products, not just those identified by the Secretary of Health and Human Services to be essential for the protection of the American public. Such a broad extension of patent life and market exclusivity will amount to billions of dollars in lost savings to the purchasers of prescription drugs in this country – most notably would be the Medicare and Medicaid programs. Similarly, this open-ended definition seems to expand the provisions of the bill providing the pharmaceutical industry with immunity from liability.

Despite its many gifts to brand pharmaceuticals, this legislation does not assure the American public that an actual product will be delivered to the federal government for stockpiling and eventual use in a case of emergency. Should it become clear that further

incentives beyond the Project BioShield Act of 2004 are truly needed to provide for the safety of the American people against bioterror threats, I am hopeful that we can address the matter with circumscription, striking a careful balance between encouraging development of much-needed new countermeasures and encouraging development of a pharmaceutical market that is fair to the American consumer. I look forward to hearing the testimony of our witnesses.

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Creating a BioDefense Industry: BioShield II

Testimony by
Senator Joseph Lieberman
Before the
Senate Judiciary and Senate HELP Committees

October 6, 2004

Creating a BioDefense Industry: BioShield II

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Before the Senate Judiciary and Senate HELP Committees
October 6, 2004

Chairman Hatch, I am pleased to be here today continuing to work with you on these critical bioterrorism preparedness issues. You understand the urgency and complexity of these matters. There is no Member of the Senate who matches your expertise on biomedical research and development issues, intellectual property and liability protections, tax incentives for entrepreneurs, and FDA regulatory and bioethics issues. You have a powerhouse staff. I could not have a better, more influential and respected partner for the bills that we've introduced. Your leadership – exemplified by this hearing – is impressive and welcome.

Chairman Gregg, your leadership in enacting Project BioShield was exceptional. You demonstrated a real command of the complex issues we face in engaging the biopharma company as part of our national defense infrastructure. You have a powerhouse staff as well.

Senator Kennedy, you have been a leader on public health issues for many decades. The many prominent biotech companies in Massachusetts view you as champion who understands their issues. Your staff has always been considered to be one of the best on the Hill.

Senator Leahy, you and your staff were targets of the October anthrax attack. Fortunately, the letter was intercepted before it reached your office, making this a personal issue for you and your staff. You understand the threat posed by these pathogens.

Working together, there is nothing the four of us can't accomplish in terms of bioterrorism preparedness. Enacting BioShield II should be our next step.

10/15 – Bioterrorism's 9/11

None of us on the Hill – especially those of us with offices in the Hart Building – will forget October 15, the date of the anthrax attack on Senator Daschle's office. This date is the bioterrorism equivalent of September 11. We also need to remember October 5, the third anniversary of the 2001 anthrax death of Bob Stevens, a photo editor at American Media in Boca Raton, Florida, and November 17, the third anniversary of the discovery of a similar anthrax laced letter mailed to Senator Leahy. Similar anthrax attacks during these weeks were directed at NBC, ABC, CBS and other news organizations. All told five people died and thousands who might have been exposed were put on Cipro, including many of us and many of our staff.

This attack on civilians with weapons grade anthrax was unprovoked. And unlike the case with the 9/11 attacks, we still don't know who mailed the anthrax letters. As with the 9/11 attacks, we were totally unprepared for the anthrax-laced letters. We are responding forcefully to the 9/11 attacks – the commission that Senator McCain and I proposed has issued a superb report and the Government Affairs Committee, where I serve as the Ranking Democrat, is hard at work translating its recommendations into legislation. Unfortunately our response to the 10/15 anthrax attack has not been as forceful.

Unlike our response to 9/11, we have not seemed to consider the 10/15 attack to be the equivalent of a declaration of war. While we have taken a few constructive steps to strengthen our Bioterror defenses, we remain painfully vulnerable to another Bioterror attack, or a chemical or radiological attack.

Timeliness of Hearings

The issue in this hearing could not be more timely: Have we done enough in enacting BioShield to ensure that we will secure the development of the medical countermeasures we need in the event of an attack, what metrics are we applying to determine whether BioShield is sufficient, and, in the event that BioShield does not accomplish enough, what policy options exist for strengthening our effort with BioShield II.

It is not too early to ask these questions; this is urgent and long-term research. It often takes ten or more years to bring a new therapeutic to market and some of the research – particularly on new antivirals – may take many more than ten years. Stocks of bioweapons developed by the former Soviet Union might fall into the hands of terrorists. We know that terrorist groups are intensely interested in acquiring Bioterror weapons and they will have no compunctions about using them.

We can't wait several years to determine if BioShield is sufficient. We need to set clear metrics of its impact and take decisive action to move to enact BioShield II if that proves to be necessary.

Many of us believe that BioShield is a step in the right direction, but we don't believe that BioShield is sufficient. If we listen carefully, we will hear that the biopharma industry — which is hiding on this issue — is saying that BioShield is not enough. So we already have strong warning signs that more needs to be done. And Senator Hatch and I – and hopefully Senator Gregg and Kennedy – will shortly be introducing BioShield II, a bill to set the terms of the debate just as our earlier bill served as the source for BioShield. This hearing starts the process for considering these additional legislative measures.

Nature of the Bioterror Threat

There is no terror threat greater than that of Bioterror. With an attack with a plane, a chemical attack or a radiological dispersion device (a dirty bomb), the loss of life can be catastrophic, but the perimeter of the attack is fixed. With an infectious disease, the perimeter of an attack might grow exponentially as the infection spreads. It is possible to kill thousands with a bomb, chemical or radiation, but it is possible to kill millions with a Bioterror pathogen.

In the 2001 anthrax attack, the terrorist wrote a note in the letter to Senator Daschle that said, "09-11-01. You can not stop us. We have this anthrax. You die now. Are you afraid? Death to America. Death to Israel. Allah is great." If this note had not been included in the letter, and if the intern who opened the letter hadn't been suspicious, it is possible that some Senators and many Capitol Hill staff from our offices — perhaps hundreds — might have died. We would only have discovered the attack in hospital emergency rooms, where Cipro might have proven to be ineffective. Cipro works as a prophylaxis only when it catches anthrax early, before the toxins are released into the bloodstream, which can happen within 24 hours of an infection. Our current anthrax vaccine is administered in six shots over 18 months.

The 9/11 Commission report states that al Qaeda "was making advances in its ability to product anthrax prior to Sept. 11" and cited former CIA Director George Tenet as warning that an anthrax attack is "one of the most immediate threats the U.S. is likely to face." Russia developed dozens of strains of anthrax and the security at these former bioweapons laboratories is suspect. It is estimated that a mason jar of anthrax spores sprayed over an urban area could infect 400,000 residents, and if undetected until they started showing up in emergency rooms, kill half of them. It is also estimated that one hundred anthrax laced letters could cross contaminate thirty million letters and infect 10,000 people with anthrax. Imagine what would happen if our mail system – which processed over 200 billion pieces of mail last year – were closed for a few months. What we need, and don't yet have, is a therapeutic that disarms the anthrax toxins at a late stage of the disease — which is the aim of a pending RFP at the Department of Health and Human Services (see below).

We saw the potential for morbidity and mortality, and massive economic disruption, with SARS. When SARS was rampant, Beijing, Hong Kong and Shanghai closed down. Quarantines were imposed and China authorized the death penalty on anyone who willfully spread the disease. During the epidemic, there were reports that the SARS virus was mutating to become more virulent. In China's countryside, fear of SARS has led to some villages setting up roadblocks to keep away people from Beijing and at least four riots against quarantine centers have been reported in recent days. Thousands were quarantined in China. In the end SARS spread to thirty countries on five continents, sickening nearly 9,000 and killing 850. SARS is a zoonotic disease that apparently can jump back and forth between animals and man, which makes it much more difficult to eradicate it. We may not have seen the last of it.

We can also remember the devastating impact of the 1918 Spanish flu pandemic that killed more than died in the first World War, about 30-40 million people (equivalent to 100 million today). In the month of October, 1918, 200,000 Americans died of the disease, 43,000 soldiers died, and 28% of our population was infected. The flu's lethality rate was only 2.5%; the lethality rate of the most common form of smallpox, variola major, is 30% and for hemorrhagic smallpox it approaches 100%. The lethality rate for SARS was about 15%. If the 1918 flu pandemic killed the equivalent of 100 million people, think of how many smallpox or SARS — both of which could be weaponized by terrorists — could kill.

Public health authorities are concerned about the incidence of avian influenza in humans. There is now concrete evidence that this virus can be transmitted human-to-human.[1] When humans contract the pathogen from birds, the death rates are very high; a majority die. Since January 2004, a total of 23 confirmed human cases of avian influenza A (H5N1) virus infections have been reported in Vietnam with 19 deaths and 12 cases in Thailand with 9 deaths. These cases were associated with widespread H5N1 poultry outbreaks that occurred at commercial and small backyard poultry farms. Since December 2003, nine countries have reported H5N1 outbreaks among poultry. More than 100 million chickens have been culled in an effort to stop the outbreak. The virus now appears to be able to infect mammalian hosts, including pigs and cats, an unusual prowess for an avian virus. This raises concern as pigs are also hosts of human flu viruses and this could yield a hybrid avian flu strain that can be passed human-to-human. The avian flu virus apparently is now carried by migratory birds so it may be very difficult to eradicate the virus.[2] We have no vaccine for the disease and the one therapeutic — Tamiflu — is only effective if given very early after the onset of symptoms. It is feared that the virus might evolve resistance to Tamiflu. Public health officials believe that in theory the avian flu could cause a "pandemic killing millions of people worldwide, and possibly hundreds of millions."[3] Whether H5N1 could be used as a Bioterror weapon against agriculture or humans is not known.

In 1947 there was an outbreak of smallpox in New York City. Eventually two of the twelve who were infected died. But the smallpox vaccination campaign was massive — 500,000 New Yorkers received smallpox vaccinations the first day and eventually 6.35 million were vaccinated in less than a month, 85% of the city's population. . President Truman was vaccinated prior to a trip to New York City.

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[1] A case in Thailand might be confirmed as the first human-to-human transmission of the virus. See Keith Bradsher, "Experts Confront Major Obstacles in Containing Violent Bird Flu," New York Times, September 30, 2004 at A-1.

[2] "Lethal Bird Flu Reemerges in Four East Asian Countries," Washington Post, September 15, 2004 at A21.

[3] See "Thais Suspect," Footnote 3. Bradsher states, "Many scientists think that an avian influenza strain that jumped to people was responsible for the Spanish influenza of 1918 and 1919, which is believed to have killed anywhere from 20 million to 100 million people t a time when the world had a quarter of its current population."

If we suffered another smallpox outbreak, it is not likely that a vaccination campaign would go so smoothly. It is now estimated that if the current smallpox vaccine were deployed in the United States 350 to 500 individuals might die from complications. The current vaccine is not recommended for patients who have eczema or are immunosuppressed, HIV-positive or are pregnant. Even worse, based on a 1971 accidental release of smallpox from a Soviet bioweapons laboratory, some speculate that the Soviets successfully weaponized a rare and especially lethal form of smallpox, hemorrhagic smallpox (with near 100% lethality).[4]

Mother Nature's pathogens are dangerous – smallpox, anthrax, plague, tularemia, glanders, typhus, Q fever, Venezuelan equine encephalitis, brucellosis, botulinum toxin, dengue fever, Lassa fever, Russian spring-summer encephalitis, Marburg, Ebola, Bolivian hemorrhagic fever, Argentinean hemorrhagic fever and fifty other pathogens could kill thousands or even millions. But on the horizon are more exotic and deadly pathogens.

We have reports that the Soviet Union developed genetically modified pathogens such as a hybrid plague producing diphtheria toxin. This manipulation increased virulence and made the plague microbe more resistant to vaccine. Other possibilities include a Venezuelan Equine Encephalomyelitis-plague hybrid is a combination of the virus and the bacteria; we have no idea what symptoms such a pathogen would manifest or how we might diagnose or treat it. Other hybrid pathogens might be developed, including a Venezuelan Equine Encephalomyelitis-Ebola hybrid.

We have reports that the Soviet Union developed a powdered form of Marburg (a hemorrhagic fever where every cell and organ of the victim bleeds). Symptoms of Marburg include kidney failure, recurrent hepatitis, inflammation of the spinal cord, bone marrow, eyes, testes, and parotid gland, hemorrhaging into the skin, mucous membranes, internal organs, stomach, and intestines, swelling of the spleen, lymph nodes, kidneys, pancreas, and brain, convulsions, coma and amnesia.

Genetically modified pathogens are another possibility. In 2001 the Journal of Virology[5] reported that Australian scientists seeking to create a contraceptive for mice used recombinant DNA technology to introduce Interleukin 4 into mousepox and found

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[4] See Dr. Alan Zelicoff's chapter "An Epidemiological Analysis of the 1971 Smallpox Outbreak in Aralsk, Kazakhstan," in Occasional Paper No. 9, *The 1971 Smallpox Epidemic in Aralsk, Kazakhstan, and the Soviet Biological Warfare Program*, edited by Jonathan B. Tucker and Raymond A. Zilinskas, June 2002 and CNS response by Dr. Serguei Popov, former Soviet bioweapons researcher, where he states, "In particular, there was a high interest in creating strains of hemorrhagic smallpox virus using the new methods of molecular biology."

[5] Jackson RJ, Ramsey AJ, Christensen DC, et. al. "Expression of Mouse Interleukin-4 by a Recombinant Ectromelia Virus Suppresses Cytotytic Lymphocyte Responses and Overcomes Genetic Resistance to Mousepox," Journal of Virology 2001: 75: 1205-10.

that it created an especially virulent virus. In the words of the scientists, "These data therefore suggest that virus-encoded IL-4 not only suppresses primary antiviral cell-mediated immune responses but also can inhibit the expression of immune memory responses." This public research suggests that introducing IL-4 can create an Andromeda stain of a virus, information of potential use to terrorist sociopaths. In addition, published studies describe how to create a recombinant vaccina virus to induce allergic encephalomyelitis in rabbits (and potentially - highly lethal smallpox virus capable of causing paralyses in humans) and how to synthesize the polio virus in a biochemical laboratory .

Other possible pathogens – some of which the Soviet worked on[6] – include antibiotic resistant pathogens. The Soviets apparently developed a strain of plague resistant to ten different antibiotics, and a strain of anthrax resistant to seven different antibiotics. Some claim the Soviets developed a strain of anthrax resistant to the current U.S. anthrax vaccine. A part of this research in a hamster model was published in Vaccine, so this information is available to terrorists.[7]

Other exotic pathogens might include autoimmune peptides, antibiotic induced toxins, and bioregulators and biomodulators. An autoimmune peptide might stimulate an autoimmune attack against the myelin that sheaths the target's nerve cells.[8] Antibiotic induced toxins are hybrid bacteria-viruses where antibiotics administered to treat the bacterial infection stimulate the virus to release a deadly toxin; the greater the doses of antibiotics, the more toxins are released. Bioregulators and biomodulators are synthetic chemical that bond to and disrupt receptors that govern critical functions of the target, including nerve, retinal, liver, kidney, heart, or muscle cells to cause paralysis, blindness, schizophrenia, coma, or memory loss.[9]

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[6] See November 1, 2000 interview of Serguei Popov, former Soviet bioweapons researcher to the Journal of Homeland Security in the appendix.

[7] See Pomerantsev AP, Staritsin NA, Mockov YuV, Marinin LI., Expression of cereolysine AB genes in Bacillus anthracis vaccine strain ensures protection against experimental hemolytic anthrax infection. Vaccine (Dec. 1997 Dec; 17-18 and 1846-50.

[8] See "A Virus-Induced Molecular Mimicry Model of Multiple Sclerosis," which shows that a naturally infectious virus encoding a myelin epitote mimic can directly initiate organ specific T-cell mediated autoimmunity – a line of research the Russians were pursuing more than ten years ago. Olson JK, Croxford JL, Calenoff MA, Dal Canto MC, Miller SD, J Clin Invest, July 2001, Volume 108, Number 2, 311-318.

[9] See "The Looming Threat: Bioweapons are much more prevalent and virulent than most of us realize. And we have little defense," Mark Williams, Acumen, Volume 1, Number IV. Some of the examples of this research were published in the Soviet scientific literature. See Borzenkov VM, Pomerantsev AP, Pomerantseva OM, Ashmarin IP., Study of nonpathogenic strains of francisella, brucella and yersinia as producers of recombinant beta-endorphin [Article in Russian], Bull Eksp Biol Med. (June 1994; 117(6) at 612-5).

Some of these might be available now from the 60 bioterror research laboratories maintained by the Soviet Union. Eventually, terrorists might be able to set up full-blown biotechnology laboratories. Rogue states could do so and they might then transfer bioweapons to terrorists or lose control of them. Over the long term, as the power of modern biotechnology grows, the Bioterror threat will grow and increasingly virulent and exotic weapons might become threats.

In November 2003 the CIA's Office of Transnational Issues published "Our Darker Bioweapons Future," which stated that the effect of bioengineered weapons "could be worse than any disease known to man." The rapid evolution of biotechnology makes monitoring development of bioweapons extremely difficult. Some of these weapons might enable the development of "a class of new, more virulent biological agents engineered to attack distinct biochemical pathways and elicit specific effects, claimed panel members. The same science that may cure some of our worst diseases could be used to create the world's most frightening weapons." It specifically mentioned the possibility of "binary BW agents that only become effective when two components are combined (a particularly insidious example would be a mild pathogen that when combined with its antidote becomes virulent)"; "designer" BW agents created to be antibiotic resistant or to evade an immune response; weaponized gene therapy vectors that effect permanent change in the victim's genetic makeup; or a "stealth" virus, which could lie dormant inside the victim for an extended period *before* being triggered.

Illustrating the speed with which biotechnology is advancing to create new bioterrorism threats is a recent announcement by Craig Venter and his Institute for Biological Energy Alternatives that in fourteen days they had synthetically created working copies of the known existing bacteriophage virus Phi X174. Other researchers had previously synthesised the poliovirus, which is slightly bigger, employing enzymes usually found in cells. But this effort took years to achieve and produced viruses with defects in their code. So the timescale has shifted from years to weeks to make a virus. There are other bigger viruses that would require more time to assemble. Venter asserts that his team could make a bacteria with about 60 times larger genome from scratch within about a year of starting. Does this mean that the debate about whether to destroy smallpox virus stocks is pointless because any virus or bacteria whose DNA sequence is published is eventually going to be easily creatable by labs all around the world?

These pathogens might be deployed by terrorists, sociopaths or rogue states that have no compunctions about killing massive numbers of "infidels" or enemies in the West. They would be experience great joy in sowing widespread panic, injury and death in America. Osama Bin Laden's spokesman, Sulaiman Abu Ghaith, bragged that al Qaeda has "the right to kill 4 million Americans" in response to deaths he claims the west has inflicted on Muslims. We are facing sociopaths with no compunction about using whatever weapons of mass destruction they can develop or secure. They would see the

potential to unleash a weapon in North America and trust that our borders would be closed so that it would only rage here and not spread to the Muslim world.[10]

Economic Consequences of an Attack

The Brookings Institution estimated that a Bioterror attack would cause one million casualties and inflict $750 billion in economic damage. An earlier Office of Technology Assessment found that there might be three million casualties. If there are this many casualties, what can we expect in the way of public panic and flight? A 2004 poll finds that "most Americans would not cooperate as officials would expect them to during a terrorism incident."[11] Only 2/5 said that they'd "follow instructions to go to a public vaccination site in a smallpox outbreak" and only 3/5 would "stay in a building other than their own home..." A vivid vision of what an attack might look like is found in Albert Camus' The Plague, with its incinerators and quarantine camps. We can review the history of the Black Death, which killed up to one of half of Europe's population between 1348 and 1349.

Imagine what would happen if the attack involves a pathogen for which we have no diagnostic, vaccine or therapeutic. If we resorted to quarantines, what would the rules of engagement be for the police and military forces we deploy to enforce it? Would it be possible to establish an effective quarantine if there is mass panic and flight? Would our hospitals be overwhelmed by the "worried well"? Would public health workers continue to serve or also flee? If our hospitals are contaminated, where would Americans receive medical care for non-terror related emergencies?

What would happen if a Bioterror, chemical or radiological attack closed Atlanta's Hartsfield International Airport – which handled nearly eighty million passengers last year? Or what would happen if we put a hold on the one hundred and twenty million international airline arrivals and departures we see each year? What would happen if we were forced to close our borders with Mexico and Canada – with 500 million crossings last year? What would happen if we restrained the 2.79 trillion automobile passenger miles driven in the U.S., one billion of which exceeded 100 miles?

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[10] All of the incentives we've proposed in our bills go to the development of medical countermeasures to weapons of mass destruction, including biological nuclear /radiological and chemical agents. While everyone is surely aware of biological countermeasures like smallpox vaccine, it is somewhat misleading to call this legislation "BioShield." We also need to develop drugs and other countermeasures to radiation and chemical exposure. In point of fact, there are a number of such countermeasures now in advanced stages of development, including at least one compound that rebuilds bone marrow destroyed by exposure to radiation. We need to be sure to apply these incentives to all of these medicines, not just medicines to prepare us for a Bioterror attack.

[11] "Most in U.S. Don't Trust Government in Attack," Washington Post, September 15, 2004 at A16.

What would happen if a terror attack rendered certain types of business activity uninsurable? What will happen if large swaths of residential real estate – none of which is currently insured for acts of terror – were contaminated and rendered worthless with anthrax spores?

Near Total Lack of Medicines

We are vulnerable to a Bioterror attack in many ways, but one of the most troubling is that we have essentially none of the diagnostics, therapeutics and vaccines we need to treat those who might be exposed or infected. If we don't have these medicines, we are likely to see quarantines and panic, which will amplify the damage and disruption. My office is on the 7th floor of the Hart Building, immediately above Senator Daschle's office. We were told if we immediately started a course of treatment with Cipro we would not die, so there was no panic. Think what would have happened if the government had said, "We don't know what this is, it's deadly, we have no way to tell who has been exposed, and we have no medicines to give you."

In the summer of 2000 the Defense Science Board found that we had only one of the fifty-seven diagnostics, drugs and vaccines we most need to respond to a Bioterror attack (we had a therapeutic for chlamydia psittaci, a bacteria). It projected that we'd have twenty of the fifty-seven within five years and thirty-four within twenty years. But today we have only two of the fifty-seven countermeasures (we now have a diagnostic for anthrax).[12]

At this rate of developing these medical countermeasures, we won't have twenty of them available until 2076 and we won't have thirty-four until 2132. This list does not include antibiotic resistant pathogens, hybrid pathogens, genetically modified pathogens, and a host of other exotic Bioterror pathogens.

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[12] The DSB "stoplight chart" – The Projected Evolution of Diagnostics, Vaccines, and Therapeutics Against Major Bioagents with Strategic R&D and Supply Actions – gives a "green" light for diagnostics where there is a "treatment available," a "yellow" light where "treatments available.Production and/or use limitations" and a "red" light where there is "no approved treatment." For a diagnostic a "green" light is given for "diagnosis < 12 hours, no confirmatory testing, asymptomatic detection," a "yellow" light for "diagnosis 12-24 hours, may require confirmatory testing, some asymptomatic detection," and a "red" light for "diagnosis in more than 24 hours, require confirmatory testing, must be symptomatic." For vaccines, the DSB gives a "green" light to "generally available," a "yellow" light if "vaccine available, production and/or use limitations," and a "red" light for "vaccine not available." This scheme explains why the DSB gives a "yellow/red" light to the current smallpox and anthrax vaccines. It gives a "red" light for diagnostics, vaccines and therapeutics for plague, Burholderia mallei, B. pseudomallei, and clostridium perfingens. It gives two red lights for tularemia, brucellosis, salmonella, eastern equine encephalitis, and Venezuelan equine encephalitis.

Little Sense of Urgency

The Congress and Administration have not responded to the anthrax attack with an appropriate sense of urgency, especially with regard to the development of medicines. We have not responded with a crash industrial development program as we did when we developed radar during the Second World War or as we are now undoubtedly undertaking to detect roadside bombs. Reluctantly, I would characterize our national response as lackadaisical.

December 4 is the third anniversary of my introduction of legislation to provide incentives for the development of medical countermeasures – including diagnostics, therapeutics and vaccines — for Bioterror pathogens (S. 1764). Chairman Hatch, October 17 is the second anniversary of our introducing our first bill together on this subject (S. 3148) and we introduced our current bill on March 19 of last year (S. 666). Twenty months ago President Bush proposed Project BioShield, a bill based on one of the twelve titles in our bills, and it was finally enacted into law on July 21. If we enact one of the titles of our bill every two years, it'll take 22 more years to complete our legislative work.

The critical issue for this hearing is whether Project BioShield, Public Law, Public Law 108-276, is sufficient or whether we need to supplement it with BioShield II, a bill that you and I intend to introduce this Fall. BioShield is only one title of our proposal – the title that provides that the government will define the size and terms of the market for a Bioterror countermeasure in advance before a biopharma companies puts its own capital at risk. This is a necessary first step; companies won't risk their capital to develop a product unless they can assess the possible rate of return (product sales) on their investment.

Enacting BioShield is a step in the right direction. If we were to enact only one idea first, this is the right first step. We will now see how the Department of Health and Human Services implements this law. We will see what R&D priorities it sets, whether it projects a market for these products sufficiently large to engage the better biopharma companies in this research, and whether it sets contract terms that company Chief Financial Officers find acceptable.

Unfortunately, we all heard a deafening silence from biopharma industry — the target of this legislation — as BioShield was being considered. The industry did essentially nothing to fix the Administration's draft – which the industry privately stated was laced with dysfunctional provisions. The industry did essentially nothing to pass BioShield. And the industry has said essentially nothing since BioShield was enacted.

It is clear to me that BioShield is not sufficient to secure development of the medical countermeasures we need, indeed, I believe it is woefully insufficient.

Basis for Industry Skepticism

The industry is skeptical that the government will be a reliable partner during the development of Bioterror countermeasures. The basis of its skepticism runs deep.

The industry points to the Cipro procurement as a case in point. In 1999, before the anthrax attack, Bayer, the developer of Cipro, was asked by FDA and CDC to secure a label indication for Cipro for anthrax. The government wanted to have one antibiotic available that was explicitly labeled for anthrax – it understands that patients might be reluctant to take a medicine for anthrax where it is not labeled for this indication. Bayer incurred the expenses to do this with no expectation of ever utilizing the product in this manner, and when the attack occurred, Cipro was the only therapeutic with a label indication for anthrax. Bayer handled this emergency with honor. It immediately donated huge stocks of Cipro, 2 million tablets to the Postal Service and 2 million tablets to the Federal government to be used to protect those who might have been exposed or infected. The government then sought to procure additional stocks of Cipro and demanded that Bayer sell it as one-fourth the market price. Threats were made by Members of Congress that if Bayer would not agree to this price the government might step in to challenge the patent for Cipro. Bayer readily agreed to the deep discount. We can assume that every other purchaser of Cipro then demanded this same price and that this cut Bayer's market return for Cipro. To add insult to injury, Bayer has had to defend itself from lawsuits by those who took Cipro in response to the attack even though it did what was asked, provided more than enough free product to treat all patients and greatly reduced it's stockpile pricing. Bayer also was deeply concerned with employee and plant security risks when it was publicly identified as the sole source of this counter-bioterrorism agent.

The industry view this incident as proving that with regard to bioterrorism research, no good deed will go unpunished. If a large pharmaceutical company can be manhandled this way, what would happen to a small biotechnology company? The industry expects that if there is an attack, and the company has the indispensable medicine we need to respond to it, the government is likely to steal the product. The industry is deeply skeptical of the government already. It has very complex and often contentious relationships with other HHS agencies, including the Center for Medicare Services, the Food and Drug Administration, and the National Institute of Health. It has constant battles with state Medicaid agencies. This is not an industry that trusts government.

Some in Congress have proposed legislation that feed industry fears. In 1994 and 1995 legislation was introduced in the House (H.R.4370, introduced on May 10, 1994, and H.R.761, introduced on January 31, 1995) that provided the government with eminent domain power with regard to AIDS to confiscate "all potential curatives and all data...regarding their development," including the patents for such compounds. Similarly, in 1999 and 2001 legislation was introduced in the House (H.R.2927, introduced on September 23, 1999, and H.R.1708, introduced on May 3, 2001) that provided for the compulsory licensing of "any subject invention related to health" where the government finds it "necessary to alleviate health or safety needs" or the patented

material is "priced higher than may be reasonably expected based on criteria developed by the Secretary of Commerce." Legislation has been introduced that would deny the benefits of the R&D tax credit for research by pharmaceutical companies where the products that arise from that research are sold at higher prices abroad than in the United States. See H.R.3665 introduced on February 15, 2000.

The industry response to these threats to its patents must be seen in light of the events of March 14, 2000. On that day a White House spokesman apparently indicated that the government might move to challenge some biopharma industry patents for genes. The industry lost $40 billion in market capitalization in the panic that ensued on Wall Street. That was not only the beginning of a deep drought in biotech company financing, it was the beginning of the collapse of the entire NASDAQ market. A similar collapse and drought had occurred in 1993-1994 the Clinton Administration proposed that the prices of "breakthrough drugs would be reviewed by a special government panel.

The issue of price controls and patents was recently considered and rejected by NIH in response to a petition for the government to march-in on the patent of Abbott Laboratories for ritonavir (sold under the name of Norvir), an AIDS therapeutic. The petitioner, Essential Inventions, asked that the government cancel the license of this patent to Abbott, which it alleged was charging too much for Norvir. The petitioner had also been involved in the 1994-1995 NIH proceeding, where NIH reviewed the impact of its 1989 protocol to review whether "reasonable" prices were being charged by companies that had licenses with NIH. NIH found that this price review process was destroying the NIH technology transfer program – companies simply would not enter into agreements with NIH. As a result, NIH repealed the price review process. The new march-in petition raised essentially the same issues and if the petition had been granted, we could have expected that the NIH tech transfer process will be crippled – again, as it was from 1989-1995. In rejecting the petition, NIH did not state, however, that is has no right to march-in based on the price of a product, implying that it could or might assert such power in the future. This can only have a chilling impact on companies considering entering into biodefense procurement and research agreements.

Aside from fears about government actions, we could not have picked a worse time to ask the industry to undertake a whole new portfolio of research. The biotech NASDAQ index stood at 1380 and it now stands at about 725. The Amex biotech indexed peaked at 801 and it now stands at about 525. The Dow Jones pharmaceutical index peaked at 420 and it now stands at about 275. The biotech industry raised $32 billion in capital in 2000 and only $16 billion last year. In June of this year, 36% of the public biotech companies had stock trading at less than $5 per share. There were 67 biotech IPOs in 2000 and only 7 last year. The industry losses each year continue to run to $4 billion. The National Venture Capital Association reports that only 2% of venture money went into biodefense following the October anthrax attack.

Of the 506 drugs publicly disclosed to be under development by the 22 largest pharmaceutical companies, only 32 are for infectious disease and half of these are aimed

at HIV/AIDS. In 1967 we had 67 vaccine companies and in 2002 we had 12. World wide sales vaccines is about $6 billion, but the world wide sales of Lipitor are $10 billion.

In addition, it is not clear whether the government is able or willing to provide the industry with the operating margins – profits – it sees for its other products.[13] The operating margin for successful biopharma companies is 2.76 to 3.74 times as great as the operating margins for major defense contractors. This means that the defense contractor model will not work to engage biopharma companies in developing medical countermeasures for bioterror agents. Whether the successful bipharma companies are "too profitable" is a separate issue. The issue addressed here is the operating margin that successful biopharma companies seek and expect as they assess lines of research to undertake. If the operating margin for biodefense research is less, or substantially less than the operating margin for non-biodefense research, it is not likely that these companies will choose to undertake biodefense research. This research is a voluntary undertaking putting their capital at risk; there is no requirement that they do this when the prospects for profits are not competitive with that from other lines of research.

Mostly we are seeing the industry hiding, not commenting on the pending legislation, not participating in the legislative process, and making every effort not to seem to be unpatriotic or greedy. Companies do not say in public that they are disinterested. They will not say what package of incentives would be sufficient to persuade them to take up biodefense work. They fear a debate on patents. They feel besieged by the current drug import debate, pressure from CMS over drug prices, and the debate over generic biologics. While I understand these fears, we simply have to know what it would take in the way of incentives to establish a biodefense industry. If the incentives in BioShield or BioShield II are not sufficient, we need to know what incentives are sufficient. We need to know what reassurances would persuade the industry that what happened to Bayer will never happen again. And only the industry can give us a clear answer to these questions. We cannot have a dialogue on these urgent national questions without the government listening and the industry speaking.

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[13] The operating margin for the major defense contractors was 8.5% in 2001 and 9.5% in 2002. The operating margin for the successful biotechnology companies listed was 31.8% in 2001 and 28% in 2002. This operating margin is 3.74 times and 2.91 times as great for 2001 and 2002 respectively as the operating margin for the major defense contractors. The operating margin for the successful pharmaceutical companies was 29.5% in 2001 and 26.5% in 2002. This operating margin is 3.47 and 2.76 times as great for 2001 and 2002 respectively as the operating margin for the defense contractors. Operating margin is profit before tax. The operating margin for the defense contractors has been adjusted for good will. Operating margin is calculated by dividing a company's operating profit by net sales. It is also known as operating profit margin or net profit margin. Operating profit it typically assessed before taking into account interest and taxes. Source: Compiled from publicly available information with assistance from Michael King, Banc of America Securities LLC.

Shifting Risk to the Industry

The goal of BioShield II is to shift the risk of countermeasure research and development to the industry. Given the skepticism of the industry about the reliability of the government as a partner, shifting the risk to the industry — with it risking its own capital to fund the R&D — will be difficult. But engaging the industry as entrepreneurs, rather than as defense contractors, is likely to be less expensive for the government and it's much more likely to secure the development of the medicines that we need.

If the government funds the research, the industry can expect to receive the operating margins that are typically paid to defense contractors – 8.5-9.5%. If the industry risks its own capital and funds the failures and cost overruns, the industry believes it would be justified demanding the operating margins that are typically paid in the commercial sector – 28-32%.

If the government funds the research, the industry expects that the government will control or own the patents associated with the medicines. If the industry funds the research, it believes it has claims on all the patents.

The only companies that are likely to accept a defense contractor model are companies with no approved products, no revenue from product sales, and no other source of capital to keep the lights on. For them government funding is "non-dilution" capital, meaning it's a form of capital that does not dilute the ownership shares of its current shareholders. Many biotech companies have stock trading in the low single digits, so they cannot issue another round of stock that would enrage the current shareholders. For them this government funding might validate the scientific platform of the company, generate some revenue, and hype the stock.

Biotech industry executives state in private that if their capital markets strengthen they will be even less likely to consider Bioterror countermeasure research. One CEO whose company has received an NIH grant for Bioterror countermeasure research stated in private that his company would never have considered this entanglement with the government if it had any other options to fund its research.

Our goal with BioShield II should be to engage the successful biopharma companies in this research — companies that have brought products to the market — and persuade them that the government will be a reliable partner. Then the risk of failure and cost overruns is shifted to the industry and we've engaged the companies with a track record of bringing products to the market. The government will need to provide substantial rewards if – and only if – the companies do succeed in developing the medicines we need, but then the government is only paying for results. When the government funds the research, it funds a process with no guarantees of any success. Providing the industry with substantial rewards for success is a model that engages the industry as entrepreneurs, drawing on the greatest strength our nation has in the war on terror.

Metrics for Success of Project BioShield

With the enactment of BioShield, it is critical for the Administration and Congress to agree on metrics for determining whether BioShield is sufficient. We also should immediately launch a comprehensive review of the policy options available to supplement it — with this hearing a perfect start for such review.

In terms of metrics to measure the success of Project BioShield, let me suggest that we are on the right track if we see the following response:

1. Government, academia and industry set a long-term research and development agenda — decades long — that is commensurate with the full range of current and evolving bioterror threats;

2. The research and development agenda focuses in part on development of powerful research tools that will enable us to respond quickly to a new, unforeseen terror agent and not just to develop countermeasures for terror agents we know about today;

3. Government determines that the key to success in developing bioterror countermeasures is securing the enthusiastic engagement of private biopharma companies pursuing the research for their own good business reasons as "profit marking arsenals";

4. Government understands and accepts the entrepreneurial culture of the biopharma industry and sees that it is not an industry that can be recruited for bioterror countermeasure research on the defense contractor model

5. Government is able to overcome the suspicions of the biopharma companies and establish itself as a reliable long-term partner in bring bioterror countermeasure research to a successful conclusion and the Government reassures industry that what happened to Bayer in the Cipro case will never happen again;

6. We begin to see that a biodefense industry has become established, with its own capital funding from investors and retained earnings, its own lead companies, its own stock analysts, and its own legitimacy in the markets;

7. Successful biopharma companies are investing hundreds of millions of their own capital in bioterror countermeasure research and competing with one another to bring countermeasures to the market, small biotech companies are able to secure funding from investors for bioterror countermeasure research, and biotech companies are able to go public with IPOs for bioterror countermeasure research;

8. CFOs of biopharma companies see a reasonable opportunity to secure operating margins (rates of return) on their investment in bioterror countermeasure research that are commensurate with those that they seek and secure for other research;

9. We see company commitments to long-term research projects that might not yield a countermeasure for the 10-12 years — the industry average;

10. Government understands that it can shift significant risk to the biopharma companies as long as it provides a reasonable rate of return if and when the companies successfully complete their research;

11. Government understands that is must remain focused on results — countermeasures that can be stockpiled and deployed — rather than process;

12. Government funded basic research is focused so that it does not compete with that of private companies and its inventions are transferred to company partners expeditiously on commercially reasonable terms;

13. Government makes the FDA animal model rule work effectively when bioterror countermeasures are brought to it for review and approval;

14. We see renewal in the U.S. vaccine industry, which has essentially been destroyed by government regulation;

15. We see companies launching major research projects to develop the next generation of antibiotics and antivirals, with major benefits for other infectious and contagious diseases, including HIV/AIDS, malaria, TB and antibiotic resistant pathogens; and

16. Government is not concerned that bioterror countermeasure research might yield collateral commercial market benefits to companies and considers this a positive development.

These are ambitious metrics for success, and I am open to hearing the Administration's own proposed metrics. What we cannot afford to do is simply to spend two years trying to implement BioShield without applying metrics of success to every stage in the process.

In terms of exploring the policy options for BioShield II, the bills that Senator Hatch and I have introduced are comprehensive and ambitious. There are other possible options that might be appropriate. We are happy to work with the Administration and appropriate committees of the Congress to review them. At a minimum, this review should focus on liability, intellectual property, tax, antitrust and research tool issues and should engage the Justice, Commerce, Treasury Departments, Homeland Security, Defense, and Health and Human Services Department.

Implementation of Project BioShield

The industry will now watch how HHS implements BioShield and how NIH responds to the march-in petition. I anticipate that the implementation of BioShield will be a painful process as HHS experiences the depth of industry skepticism about this research and this market. In fact, it's not clear which is more threatening form an industry perspective – no market or an exclusively government market. I anticipate that HHS will find that it will only be able to engage biopharma companies that have little or no success in securing development of FDA-approved products and that are dependent on government funding for the research. If HHS is able only to engage these companies, and able only to engage companies as defense contractors, it's prospects for securing development of the full range of medical countermeasures we need will be bleak.

HHS will be setting its long-term agenda of development projects. It has yet to be seen how HHS will set the mix of diagnostics, therapeutics, and vaccines. Many believe that diagnostics and therapeutics are more important priorities than vaccines. Former Soviet bioweaponeer Ken Alibek and his colleague Charles Bailey argue that "vaccines are not a realistic prophylaxis for civilian populations, because they would be only be

effective in very narrowly defined circumstances.[14] They argue that even if we had vaccines for the top six Bioterror pathogens, it is "highly unlikely that a decision would be made to vaccinate the entire population against each" of them. They argue that vaccines are "unlikely ever to be used…" They recommend we focus on medicines to treat the late stages of these diseases. Given the delay that may arise between an attack and the recognition of it as an attack, this would seem to be the most important priority for BioShield.

One key implementation issue has already arisen. My staff has heard that HHS is saying that it won't guarantee procurement of a medical countermeasure under BioShield unless the FDA has granted IND (investigational new drug) status to the medicine. It has referred companies to NIH for funding to take the product to that stage of development. This interpretation makes no sense and may substantially inhibit the effectiveness of BioShield. The concept behind BioShield is that the government will provid detailed specifications regarding the market for a medical countermeasures so companies can assess whether to risk their capital to develop the countermeasure. This concept applies to research and procurement of any medicine, including those that are long-term research projects that might take many years to reach the IND stage. Because BioShield is a procurement bill, not a research funding bill, and only guarantees procurement if and only if the country develops the product the government needs, there is little risk in applying BioShield to pre-IND research. Many companies have no interest in negotiating a research funding grant from NIH — they'd rather rely on investor funding or retained earnings — or might not receive a grant.

Perhaps this interpretation arises from the extremely limited funding for BioShield. The Tufts Center for the Study of Drug Development estimates that industry expends more than $800 million on average to develop a new chemical entity. It is clear that the $5.6 billion funding for BioShield procurement represents a fraction of what will be needed to develop all of the medical countermeasures we will need to prepare for a Bioterror, chemical or radiological attack. (By way of contrast, the government spent nearly $7 billion in just one year developing the missile defense system. Many believe we are much more likely to see a Bioterror than a missile attack.) As a way to ration its scarce funds, the IND requirement might be necessary, but as a development strategy it does not fully exploit the potential embodied in BioShield to shift the risk to the industry to fund the research in exchange for a specified reward for successful R&D projects.

The first Request for Proposal (RFP) for biodefense subsequent to the enactment of BioShield was issued on August 18[15] for immunotherapeutic antitoxins (e.g. monoclonal antibodies, polyclonal antibodies, and human immune globulin), other protein products (e.g. mutated toxins), and small molecule entity treatments (e.g. protease

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[14] Ken Alibek and Charles Bailey, "BioShield or BioGap," Biosecurity and Bioterrorism: Biodefense Strategy, Practice and Science, Volume 2, Number 2, 2004.

[15] http://www2.eps.gov/spg/HHS/OOS/OASPHEP/Reference%2DNumber%2D2004%2DN%2D01385/Attachments.html

inhibitors) for the treatment of inhalational anthrax. The RFP calls for the procurement of 10,000 -200,000 therapeutic courses of treatment, contingent upon the outcome of an initial procurement of "10 grams" of the product for the government to test – a surprisingly small amount. Many in industry found this RFP surprising, with its focus on an initial purchase of such small amounts of the product which will serve as a significant deciding factor in determining the fate of further acquisition of the product. This approach seems rather plodding, attenuated and cautious.

More troubling, there is no clear timeline for procurement of additional courses of treatment nor is there a predictable outcome for a contractor awarded only the initial phase of the contract. There seems to be no limitation on the company selling the same product in other markets, including allies or civilian markets.

The RFP indicates that even though the company, at the time of award, has obtained an IND from the FDA to proceed with human clinical trials, HHS will be reviewing the IND data on its own and conduct its own comparative testing, after which it might conclude that it will not go forward with a contract with the company. Given FDA's special expertise on these matters and their designated mission to protect public health by ensuring safety and efficacy of medical products, it is not clear what other government agency might find to trump the FDA determination. Does HHS have a specific animal model or in vitro test that they find particularly relevant, different from any communicated by the FDA during the IND process that the company hasn't performed? It is not clear why HHS requires only that the IND be filed, and not requiring that it be approved at the time of application. It is not clear in the RFP how soon HHS will make its final determination. Will it wait until the FDA has approved or denied an IND for all companies who submitted proposals, or for some subset? What if the FDA approval of the IND sets standards for the clinical trial in excess of those upon which the bid price is premised?

Other terms of the RFP are less surprising. The intellectual property associated with the product appears to remain the property of the company. The contract asks for offers from companies for the fixed total contract price (with some items being cost reimbursable that needlessly subjects the winner to implement very burdensome cost accounting processes, thus further discouraging industry participation), more than one contract might be issued, and the company must first submit a "complete IND" application to the FDA for the initiation of human clinical trails. INDs can only be obtained after the company has completed toxicity and other laboratory tests that demonstrate that the product is "reasonably safe to give to human subjects in clinical trails." The RFP requires that the company show "proof of concept in small animals." The contractor must commit to securing final FDA approval for the product. The contractor shall be required "to attempt to obtain clinical trial insurance" but can request HHS to invoke the Safety Act for the work, thereby leaving a bidder's position on liability to be tenuous at best. The company is required to establish a security plan for the development, manufacturing, storage and distribution of the product. The company is required to maintain a production line for the product through the life of the contract. The experience of the bidders is one relevant factor in determining which will be

selected. About 100 complex FAR provisions will be included in the contract, all with their own interpretations and enforcement issues. Strangely the contract takes advantage of none of the special contracting authority found in BioShield, which can be used to cut through some of burdensome and intimidating FAR contracting provisions.

In addition, many of the standard "special contract requirements" are not appropriate for biodefense contracts and should be tailored accordingly. For example, the requirement for incorporation of the technical proposal into a contract would make this information publicly available. Not only does this pose the risk of exposing proprietary data to competitors, but it also creates a national security risk, allowing potential development by terrorist organizations of strains that can evade the specific countermeasure which is being developed for stockpiling and make such countermeasure ineffective.

Responses to the RFP are due October 19, 2004 and we will then see whether this HHS approach is proving to be effective in securing the engagement of biopharma companies with a proven track record of bringing products to market. We must then wait for the first procurement under Project BioShield to go forward.

We anticipate that the implementation process will be a difficult one as HHS learns more about what terms and limitations are acceptable to the companies it wishes to bid and which are considered threatening or unduly burdensome. Given the operating margins for these companies, the fixed price for these contacts might be a huge issue. When the Joint Vaccine Acquisition Program (JVAP) at the Department of Defense put out a solicitation for the procurement of seven vaccines, not a single established pharmaceutical company chose to bid.

BioShield II Provisions

The BioShield II legislation we will introduce will be based on S. 666, legislation Senator Hatch and I introduced on March 19, 2003, and from which BioShield was taken. While BioShield establishes a predictable and guaranteed government market for medical countermeasure for Bioterror pathogens, BioShield II will include tax incentives to form capital for biopharma companies to conduct research to develop these countermeasures, protect and enhance intellectual property associated with these countermeasures and address other issues that affect the companies' inclination to conduct this research.

The premise of this legislation, as it was with BioShield, is that direct government funding of this research is likely to be much more expensive and risky to the government and less likely to produce the countermeasures we need to defend America. Shifting some of the expense and risk of this research to entrepreneurial private sector firms is likely to be less expensive and much more likely to produce the countermeasures we need to protect ourselves in the event of an attack.

The legislation will provide that a company seeking to fund research is eligible to elect from among three tax incentives:

(a). Establishment of an R&D Limited Partnership to conduct the research. The partnership passes through all business deductions and credits to the partners.

(b). Issuance of a special class of stock for the entity to conduct the research. The investors would be entitled to a zero capital gains tax rate on any gains realized on the stock.

(c). Receive a special tax credit to help fund the research

The first two provisions help small biotech companies to form capital to fund the research. These companies cannot use tax credits because they have no revenue from product sales and no income tax liability with respect to which to claim a tax credit.

The legislation will provide that a company that successfully develops a countermeasure is eligible to elect one of two patent incentives:

(a). The company is eligible to receive a patent for its invention with a term as long as the term of the patent when it was issued by the Patent and Trademark Office, without any erosion due to delays in the FDA approval process.

(b). The company is eligible to extend the term of any patent owned by the company for two years. The patent may not be one that is acquired by the company from a third party. In S. 666, this wild card patent provision is only available to companies with $750 million or less in paid-in capital.

In addition, a company that successfully develops a countermeasure is eligible for a 10-year period of market exclusivity on the data supporting FDA approval of the countermeasure.

The legislation will provide for protections against liability for the company that successfully develops a countermeasure.[16] It will grant companies with a limited

[16] One issue to address regarding liability is protection for those administering, distributing, and overseeing the administration and distribution of the Strategic National Stockpile ("SNS") and other emergency uses authorized under the Project BioShield Act. Health care providers, including health care workers and volunteers who assist them, and local government agencies and their employees are on the front lines of defense after such an attack or other emergency develops, especially in densely populated metropolitan areas. The efficient administration of prophylaxis and other countermeasures designed to prevent the spread of disease or to provide antidotes to victims of an attack or other emergency is critical. Legitimate concern about liability can seriously hamper relief efforts by health care providers, local government agencies, and a wide range of individuals.

Such liability protection currently exists for measures to prevent and treat smallpox. Section 224(p) of the Public Health Service Act, 42 USC § 233(p), provides for Federal Tort Claims Act protection for "covered persons", which include health care entities, local government agencies, and other persons and entities involved in the administration of smallpox countermeasures, including vaccina inoculation. There appears to be no reason to limit liability protection to smallpox countermeasures given what we know about the threat posed by other forms of attack, such as anthrax. The SNS

exemption from the antitrust laws as they seek to expedite research on countermeasures. It will include special incentives are incorporated to ensure that manufacturing capacity is available for countermeasures. And it will apply all of the incentives to the development of research tools.

Given the reluctance of the biopharma industry to participate in the legislative process on BioShield, it's been difficult to determine whether enactment of these BioShield II incentives will be sufficient to establish a biodefense industry. I believe that doing less will not be sufficient, but I acknowledge that even if we enact every provision in BioShield II, we may not meet all of the metrics of success that I have proposed.

We should not stop until we have reached our goal – to establish a well capitalized and expert biodefense industry to develop these medical countermeasures. We must recognize that our challenge is not simply to procure and stockpile a few diagnostics, therapeutics and vaccines. The Bioterror threat is evolving rapidly and over time we will need to develop many additional medicines. We need a biodefense industry ready, willing, and able to accomplish this mission.

To do this, we need to reassure the biopharma industry that the government will be a reliable partner in this research and persuade the industry that what happened to Bayer in the Cipro procurement will not happen to them. Most of all, we need to engage the successful biopharma companies – the ones that have a track record of bringing safe and effective medicines to market. We need to engage these companies as entrepreneurs, not as defense contractors. Acting as entrepreneurs, deploying their own or investor's capital, we can shift some of the risk of this research to the industry. If we seek to engage

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includes vaccines, antitoxins, antivirals, chemical agent antidotes and other emergency medications and supplies for a vast array of public health emergencies. Similarly, emergency uses under the Project BioShield Act potentially include other drugs, biological products and devices developed to treat, identify or prevent biological, chemical and radiological attacks.

One approach would be to apply liability protection to SNS assets and emergency uses authorized under the Project BioShield Act similar to what is currently provided for smallpox. Persons covered under the proposed amendment would be the same. Moreover, as with the protection afforded to those carrying out research and development contracts under the Project BioShield Act (section 319F-1(d)(2)-(3) of the Public Health Service Act), this approach would permit recourse by the United States in cases of gross misconduct by covered persons and authorize the Secretary of Health and Human Services to institute procedures to determine who is entitled to protection.

Unfortunately, a response to a biological, chemical or radiological attack or any other public health emergency sometimes requires broad, prophylactic measures to prevent extensive casualties or a catastrophic spread of disease not known in this country for more than 80 years. In order to be fully prepared, we must consider how to ensure that those administering, distributing, and overseeing the administration and distribution of measures to stop or mitigate the effects of such an attack or emergency are not exposed to unnecessary liability.

these companies as defense contactors, it's likely to cost more with fewer prospects for securing the development of the medicines we need.

The single most controversial proposal in BioShield II will be the wild card patent extension. There will be substantial debate on this proposal and both sides have legitimate concerns. In favor of it is the concern that without it we will not be able to establish a biodefense industry. Against it is the concern that it will unfairly raise health care costs to consumers and health care entities. The Congress has looked at similar points before and decided to extend patents on drugs as an incentive for companies to conduct pediatric clinical trials and secure appropriate pediatric labels. In this case Congress judged that the patent extensions were worth their cost. The details of how the wild card patent provision would work are also important and we are open to discussing them. In the end, Congress will have to weigh the competing considerations and judge whether we should include the wild card patent as an incentive.

If BioShield II is insufficient to accomplish these goals, we need to develop BioShield III. We must do whatever it takes to ensure that we have the medical countermeasures available if and when there is a Bioterror attack. The consequences of failing to do this could be catastrophic. We cannot settle for some effort to develop these countermeasures – we need results, not process.

Who Should Be In Charge?

BioShield is being implemented by the Department of Health and Human Services. The bills that Senator Hatch and I have introduced place the implementation responsibility with the Department of Homeland Security. The Department of Defense is a third alternative, but its efforts to develop Bioterror medical countermeasures have been a scandalous failure. We need a frank and full review of which agency has the best culture and expertise to lead this vital effort.

HHS has a complicated and often contentious relationship with the biopharma industry. The industry has had frequent policy conflicts with the Food and Drug Administration, The Center for Medicare Services and the National Institutes of Health. Over many decades we've seen HHS focused on keeping unsafe and ineffective products off the market, reducing the government reimbursement for medicines, and policies that are hostile to patents. The original version of BioShield submitted to the Congress by the Administration was laced with provisions that the industry viewed as dysfuncational, unworkable, and hostile. Given this history and culture, it is not clear that HHS can effectively work with the industry on a massive industrial development program with regard to Bioterror countermeasures. HHS does substantial scientific and contracting expertise.

The Department of Homeland Security appears to be developing a culture that focuses intensively on the bottom line with no time taken for ideological diversions. It has no history of conflicts with the biopharma industry. It does not now possess substantial scientific and contracting expertise.

The issue of who is in charge is central to all of our homeland security issues. That's why I first proposed that we create a Department of Homeland Security. We should review carefully the effectiveness of HHS in implementing BioShield, its metrics for determining whether BioShield is sufficient, and its review of the policy options for supplementing BioShield. If HHS does not perform well in these roles, we should consider whether the Department of Homeland Security might provide better leadership.

Research Tools

We will never be able to anticipate all of the pathogens that might be utilized by terrorists. Our medicine chest will never have all the medicines we need for all the possible terrorist pathogens. The ultimate and only effective bioterror defense are "research tools" powerful enough so that we can develop and deploy a new countermeasures quickly after an attack has occurred. We need this power to respond to Mother Nature's new concoctions, like SARS, but it's also the only defense against exotic terror pathogens we'll never see in advance of an attack. As stated by the leading biodefense think tank,

> The process of moving from 'bug to drug' now takes up to ten years. The U.S. biodefense strategy must act as one of its key strategic goals the radical shortening of this process.[17]

The development of research tools is a central focus of the bills that Senator Hatch and I have introduced and it will be a central focus in BioShield II and all of the incentives in BioShield II will apply to the development of research tools.

One obstacle to the development of research tools to expedite the development of Bioterror countermeasures is the NIH Research Tool Guidelines. Finalized in 1999, the guidelines[18] find that "intellectual property restrictions can stifle the broad dissemination of new discoveries and limit future avenues of research and product development." It defines a "research tool" in "its broadest sense to embrace the full range of tools that scientists use in the laboratory, including cell lines, monoclonal antibodies, reagents, animal models, growth factors, combinatorial chemistry and DNA libraries, clones and cloning tools (such as PCR), methods, laboratory equipment and machines." A more sweeping definition is hard to imagine. With regard to these tools, the guidelines find that patents, and "reach-through royalty or product rights, unreasonable restraints on publication and academic freedom, and improper valuation of tools impede the scientific

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[17] Bradley T. Smith, Thomas V. Inglesby, and Tara O'Toole, "Biodefense R&D: Anticipating Future Threats, Establishing a Strategic Environment," BioSecurity and Bioterrorism: Biodefense Stategy, Practice, and Science, Volume 1, Number 3, 2003.

[18] PRINCIPLES AND GUIDELINES FOR RECIPIENTS OF NIH RESEARCH GRANTS AND CONTRACTS ON OBTAINING AND DISSEMINATING BIOMEDICAL RESEARCH RESOURCES, Federal Register Notice published on Thursday, December 23, 1999, 64 FR 72090.

process whether imposed by a not-for-profit or for-profit provider of research tools." While the NIH guidelines only apply to recipients of government funding, the guidelines states that "it is hoped that other not-for-profit and for-profit organizations will adopt similar policies and refrain from seeking unreasonable restrictions or conditions when sharing materials."

The practical result of the guidelines is that any private company that seeks to develop research tools must be wary of working with any institution or individual that receives NIH grants. This estranges the industry from the academic community with regard to the development of these tools. In many cases, the innovative research of academics had led to the private sector development of tools by companies whose business plan was to create such tools, not develop therapeutics. Now it is much less likely that the work of academics regarding research tools will ever be commercialized. This could not be worse timing – what we need to prepare for a Bioterror attack is a well capitalized research tool industry. Accordingly, our bills waive the application of the research tool guidelines to tools relevant to the development of Bioterror countermeasures. These tools are the gold standard for preparedness for a Bioterror attack.

Finally, the Food and Drug Administration has published a rule that permits Bioterror medical countermeasures to be developed relying on tests in animals rather than humans. This is necessary as it is not ethical to test a Bioterror pathogen on a human subject and there is no patient population available with a naturally occurring incidence of these diseases. One major issue for the development of these countermeasures is whether animal models exist for the diseases for which we need to develop countermeasures. If there is no animal model for a disease, it is not likely that biopharma companies will begin a research project to develop a countermeasure when there is no path to FDA approval. In addition, there is a growing shortage of animals.[19] We need to take decisive action to ensure that this research tool does not prove to be a major bottle neck in the R&D to develop Bioterror countermeasures.

Third World Diseases and Antibiotic Resistant Pathogens

As we draft BioShield II, we are actively exploring the scientific and economic implications of applying BioShield and BioShield II to infectious diseases generally, not just pathogens deemed to be "terror weapons."

As a matter of science, the research and development on countermeasures to bioweapons is inextricably linked to research directed to pathogenic virus, bacteria and fungus that cannot be weaponized. Consequently, it makes sense to enact incentives for

[19] See Michael Hopmeier, President/CEO of Unconventional Concepts, "Too Many Germs, Too Few Monkeys: The Shortage of Non-Human Primates, Clinical Research, and Test Infrastructure," FDLI Update (March/April 2004).

research that addresses the pathology, diagnosis or therapeutics that relates to virus bacteria or fungus whether it has been or could be weaponized or not. Research on infectious diseases seeks to understand how organisms cause disease, the immune system responds to pathogens, and antibiodies and other medicines protect against them. This research is broadly applicable to both bioterror and non-bioterror pathogens. In the end, we need broad-spectrum antibiotics, anti-virals that can be utilized against a variety of viruses, and vaccines that can be adapted to a variety of organisms.

As enacted into law, BioShield could be applied to the development of new antibiotics, which can serve as a Bioterror countermeasure. The Administration's draft of BioShield provided that if there was a "significant commercial market for the product other than as a homeland security threat countermeasure" BioShield would not apply (S. 15, section 203, as introduced on March 11, 2003). This anti-dual use provision, which would have squandered the potential benefits of this legislation for the development of new antibiotics and other dual-use medicines, was deleted in the final version of the bill. We need these antibiotics as countermeasures for Bioterror pathogens and we especially need them to respond to Bioterror pathogens that are engineered to be antibiotic resistant.

We also need new antibiotics to respond to a public health crisis in our hospitals – one documented in great depth by the Infectious Diseases Society of America in Bad Bugs, No Drugs (July, 2004). IDSA finds that about 70% of the two million bacterial infections in America each year are resistant to at least one antibiotic. If our current range of antibiotics loses its effectiveness – and signs of resistance to our last line of antibiotics, vancomycin, are appearing – then we will face a public health crisis even if there is never a Bioterror attack. The relentless rise of antibiotic resistance in bacteria and the exit of all of the major Pharma companies conducting R&D in this area due to lack of incentives will leave us vulnerable in the extreme by the end of the decade. At some point society will be badly bitten by this trend, with pandemic influenza being the most likely candidate in the short term. I fear that someday we'll be forming another 9/11 commission after large numbers of Americans (and others around the world) die as a result of failure of our government to engage the problem proactively.

While BioShield could apply to the development of new antibiotics, it is not likely that new antibiotics will be listed as a priority of the Administration for Project BioShield. BioShield focuses on procurement by the government of medical countermeasures, so it is likely that it will mostly or entirely be utilized for procurement of countermeasures where the government is the sole market. There is a substantial civilian market for antibiotics, with the government only a marginal player. It makes more sense to deploy the tax, intellectual property, and other incentives in BioShield II to this research. This would both be consistent with our needs for Bioterror preparedness and provide a much-needed benefit to our public health infrastructure.

In terms of infectious disease generally, it is likely that the biopharma companies that we might engage in developing Bioterror countermeasures will have expertise, and capital from investors for research on a broad range of infectious diseases, going well beyond those that might be weaponized. In fact, it may well be easier for these

companies to form or deploy capital for this research if it involves development of medicines where the Federal government is not the sole or principal market. In the end, we need to establish an Infectious Disease Industry, not just a BioDefense Industry. We need companies capable of development effective platforms that have a broad application to a variety of infectious diseases — research tools of immense power and importance. We certainly need many more companies with expertise in developing vaccines. So, it makes little economic sense to stovepipe these lines of research, providing incentives for research to develop medicines for only a select few pathogens we label as "bioterror pathogens." It is also true that in some cases we may not know if a particular pathogen can be weaponized. For example, some believe SARS could be weaponized.

Accordingly, it makes good sense to apply BioShield II to research and development of countermeasures for "infectious" diseases even if they might not be pathogens that can be weaponized. BioShield could also be applied to these countermeasures with a proviso that the government could organize a procurement fund comprised of its own funds, funds form international public health agencies like the Global Alliance for Vaccines and Immunization (GAVI), foundation funding, and other sources. This is an issue that we need to explore with organizations such as the IDSA, The international Aids Vaccine Initiative, the Alliance for Microbicide Development, the Alan Guttmacher Institute, the AIDS Vaccine Advocacy Coalition, Biotech Ventures for Global Health, the Aeras TB Foundation, AmFAR, the Global Alliance for TB Drug Development, the Malaria Vaccine Initiative (MVI), International Partnership for Microbicides, Medicines for Malaria, and similar groups.

The need for additional research to develop therapies, cures, and vaccines for infectious disease – both Bioterror and natural – is clear. Worldwide, seventeen million deaths annually are caused by infectious and parasitic diseases, 33% of the total and 71% of all deaths among children under 5 years of age. This compares with fourteen million deaths from famines, wars, violence and aging, the same number from circulatory and obstructive pulmonary disease, and five million due to cancer. AIDS is out of control in many countries and mutating to create new strains. In the end, we may lose one hundred million people to AIDS. Malaria is developing resistance to the newest prophylaxis – with nearly three million deaths a year. Antibiotic resistant TB is surging – with over three million deaths a year. One million die each year of hepatitis B and one billion are infected. 165,000 each year die of hookworm and roundworm. We have seen waves of emerging diseases, including AIDS, SARS, West Nile virus, Lyme disease, and hantavirus. The public health agenda – for bioterrorism and beyond – is compelling and amply justifies enactment of new incentives for development of effective medical countermeasures.[20]

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[20] Incentives for research on Third World diseases have been proposed before. On May 16, 2001 Senators Kerry and Frist introduced S. 985, The Vaccines for the New Millennium Act of 2001. An identical bill was introduced in the House by Representative Pelosi on April 4 (See H.R. 1504).

S. 895 and H.R. 1504 proposed the enactment of two tax credits for research and sales of vaccines and microbicides for malaria, TB, HIV or "any infectious disease (of a

single etiology) which, according to the World Health Organization, causes over 1,000,000 human deaths annually." It did not apply to diseases with fewer deaths but much greater incidence. The new credit for research was set at 30%, which compares to the current 20% R and D Tax Credit. The bill bared any credit for any vaccine research (other than human clinical testing) conducted outside the United States. The credit was made "refundable" for corporations with "aggregate gross assets" of less than $500,000,000, zero tax liability in the preceding two years, and the corporation pledges to apply the refund to the vaccine or microbicide research. This made it useful to small biotech companies with no approved products, no sales revenue and no tax liability with respect to which to apply a tax credit. No carrybacks of the credit were permitted for research that had previously been performed. The sales tax credit was for the amount it is reimbursed sales of these vaccines and microbidies to a nonprofit organization or foreign government for distribution in a developing country. This credit makes the sales income tax exempt, increasing its value by about 35% (the marginal tax rate of most corporations). This credit was not refundable, and a $100 million limit was set on the available credit for the first five fiscal years and a $125 million limit for the next four years. This budget for the credit was to be allocated by the U.S. Agency for International Development. In addition, the legislation established a "Lifesaving Vaccine Purchase Fund," with the purchases to be made "at prices which take into account the seller's research, development, and manufacturing costs and the desirability of the vaccine purchased."

The legislation includes the following statement regarding distribution of the vaccines developed using the research credit: "Given the important goal of ensuring that all those in need, in both industrialized and developing countries, reap the benefits of any vaccine or microbicide that is developed for HIV, tuberculosis, or malaria, and acknowledging the importance of intellectual property rights and the right of corporations and shareholders of corporations to set prices, retain patent ownership, and maintain confidentiality of privileged information, corporations and shareholders of corporations who elect to take the credit under section 45E of the Internal Revenue Code of 1986, as so added, for research expenses incurred in the development of a vaccine or microbicide shall certify to the Secretary of the Treasury that, not later than the date which is 1 year after the date on which the vaccine or microbicide is first licensed, such corporation will establish a plan to maximize distribution of such vaccine or microbicide in the developing world using such mechanisms as technology transfer, differential pricing, and in-country production where possible, or other mechanisms to maximize international access to high quality and affordable vaccines." It also acknowledged that "Flexible or differential pricing for vaccines, providing lowered prices for the poorest countries, is one of several valid strategies to accelerate the introduction of vaccines in developing countries."

In 2001, Senator Kerry secured inclusion of a tax credit for research on vaccines and microbicides for tropical diseases in the Senate version of H.R. 1836, the Republican tax cut legislation. (See Section 811). The credit was for research, it was set at 30% (compared to the current R&D Tax Credit of 20%), it did not cover sales of any such vaccine or microbicide, and it was not refundable (so it could not be used by any company with no tax liability, which is 95% of the biotech industry). It was scored by the

National Institutes of Health Reform

BioShield and BioShield II are directed at the biopharma companies. These companies have the expertise and experience needed to develop medical countermeasures; government does not. There remains an important role for government funded basic Bioterror research, principally through the National Institutes of Health. We need to be sure that these basic research investments implement a sophisticated strategy, with a clear understanding of how this research supports, and does not conflict with or duplicate, research that is more appropriately conducted by the biopharma companies.

The patent restoration provisions of BioShield II are especially critical to patents on basic research. Inefficiencies in the technology transfer process and the long-lead time necessary to translate basic research into FDA-approved products means that patents on basic research tend to be eroded. The patent term runs from the date of application, not the date of FDA approval, so if there are delays between the grant of a patent and FDA approval, much of it can be lost. If a patent has eroded 3-4 years, and additional erosion can be anticipated, it is likely that the patent will never be commercialized, it will block other researchers while it is in effect, and then it will die. Unpatentable inventions tend not to be commercialized by the biopharma industry.

As Anthony Fauci, the Director of NIAID, has acknowledged that "the path to product development has not been a part of [NIAID's] research strategy."[21] NIH translates its basic research into commercial products through technology transfer licenses with biopharma companies. For a variety of reasons, including the imposition of the reasonable price clause, the threat of march-in rights, the NIH research tool guidelines and other policies, NIH's technology transfer program has not be notably successful.

A variety of measures should be considered to strengthen this critical program.

1. The commercialization efforts at NIH could be consolidated, centralized and restructured within a new National Center for Health Care Technology Development. It could be headed by a Director subject to Senate confirmation.
2. The Center's mission could be to increase the yield of our current investment in biomedical research and make the commercialization efforts more responsive to the medical needs in this country and more transparent to the taxpayers and their elected representatives.
3. The Center could oversee NIH's technology transfer programs, patenting and licensing of patents, and set a research and development strategy for NIH sponsored research.
4. The Center could gather and publish detailed measures of NIH's success in ensuring that its basic research is developed into commercial products.

Joint Tax Committee as losing $1.547 billion over ten years (See JCX-48-01)(May 24, 2001) It was deleted in the conference and did not become law.

[21] Fauci AS. Biodefense on the Research Agenda. Nature, 2003: 421: 787.

5. The Center could be the liaison with the NIH grantees on all issues involving technology transfer.

6. Restrictions could be lifted that reduce the ability of NIH to act in a more entrepreneurial manner. This will allow NIH to foster the growth, by investing in and sponsoring technology that is emerging and entering into the commercial research market.

7. NIH and each Institute could consult with an industry advisory board to insure its research agenda is supportive of and not duplicative of industry research.

8. The process for selecting grantees could include assessments of the opportunities that may exist for commercialization of the sponsored research.

9. Grantees success in bringing technology to patients could be tracked so that the successful programs might be recognized, rewarded and copied by others

10. The Center could be charged with teaching what it learns to the research community in this country and around the world.

In addition, I have proposed I have proposed creating an American Center for Cures, which would be connected with the National Institutes of Health. Its job would not be to engage in much original research, but rather to better organize and fund work already being done in government and private laboratories across the country.

Right now, there is not only duplication of effort, but efforts are uncoordinated. Different laboratories may have keys to different pieces of the puzzle and be completely unaware of each other's work.

The Center for Cures would connect these efforts.

The Center for Cures would also work with the scientific community and the private sector to support the promising lines of research, even on those drugs and antibiotics that, while unprofitable, are indispensable if it is you or a family member who need them.

When leads looked promising, the Center would be able to commission large-scale research across disciplines to take advantage of advances not only in biology, but also in the physical sciences, computer science, and engineering.

The Center for Cures would also work with the pharmaceutical and biotechnology industries – especially smaller firms – to create incentives for innovation as well as cutting through bureaucracy to make it quicker and easier to get cures from the researcher's bench to the patient's bedside.

Responding to a Declaration of War

We should not need a 9/11 Commission report to galvanize the Administration and the Congress to respond to the unprovoked and deadly Bioterror attacks of three years ago. The threat could not be more obvious and what we need to do is also obvious. If we don't develop the diagnostics, therapeutics, and vaccines to protect those who

might be exposed or infected, we risk public panic and quarantines. We have the world's preeminent biopharma industry and we need to put it to work in the national defense.

BioShield is a step in the right direction, but it is a small step that does not take us where we need to go. We need to follow the implementation of BioShield very carefully and set clear metrics for determining its effectiveness. We should not wait to begin to review the policy options available to supplement BioShield. Senator Hatch and I will be proposing BioShield II and we will press for its consideration. We should press the biopharma industry to present its views on what it will take to engage it in this research and what it will take to establish a biodefense, research took, and infectious disease industry.

The American philosopher, George Santana said, "Those who cannot remember the past are condemned to repeat it." It's only been three years since the anthrax attack but I fear our memory of it already has faded. Let this hearing stand as a clear statement that some of us in the Congress remember what happened and are determined not to permit it to happen again. War has been declared on us and we need to act as if we noticed.

Appendix

Defense Science Board "stoplight chart" – The Projected Evolution of Diagnostics, Vaccines, and Therapeutics Against Major Bioagents with Strategic R&D and Supply Actions (Summer 2000)

"Move on BioShield to Aid Biodefense Industry," Senator Joe Lieberman and Senator Orrin Hatch, The Hill (May 19, 2004)

Chronology: Incentives for Research to Develop Countermeasures to Bioterror Pathogens

Outline: Biological, Chemical, and Radiological Weapons Countermeasures Research Act of 2003, S. 666 (Senators Lieberman and Hatch)

BioPharma vs. Defense Contractor Operating Margins

Interview—Serguei Popov, Journal of Homeland Security (November 13, 2000)

Move on BioShield to Aid Biodefense Industry

Senator Joseph Lieberman and Senator Orrin Hatch
May 19, 2004 — The Hill

Anthrax hit the Senate in October, 2001 and Senators and staff took CIPRO to prevent infection. There was no panic and no one fell ill. This may have lulled us into a false sense of complacency.

In fact, we are woefully unprepared with diagnostics and medicines to respond to a bioterror attack. Four years ago the Defense Science Board found that we had only one of the 57 bioterror medical countermeasures we most need. Today we have two. If we don't have diagnostics, drugs, and vaccines, next time we could see panic. Our country simply does not have the medicines we need to respond to a bioterror assault, neither in the short term nor the long run.

So what must we do? For openers, one way we should enlist our innovative biotech industry into the business of developing diagnostics, vaccines, antibiotics, and other medical countermeasures that would control the massive disease and death we might see from a biological weapons attack. Funding basic research is no longer enough. We also need diagnostics and medicines ready to use.

Right now, our biotech industry is not conducting the necessary R&D to develop these countermeasures, primarily because there is no private sector commercial market for these products. Because we hope and pray that we'll never face an attack, government emergency stockpiles are the only market. So, we must create the equivalent of a private sector commercial market for which the bio-pharmacological industry *will want* to invest their own and investors' capital to develop bioterror countermeasures. The industry must be provided tax incentives so small biotech firms can form the capital to fund this research. It must be assured of intellectual property protections for those worried the federal government might in a crisis confiscate a countermeasure. And, it must have liability protections because many of these countermeasures cannot be fully tested in clinical trails.

Last year, we reintroduced the Biological, Chemical, and Radiological Weapons Countermeasures Research Act, an ambitious bill we first introduced in 2002 that would create the right conditions and incentives for private sector R&D on bioterror countermeasures. Once those incentives are in place, the industry and its investors would be paid if, and only if, they successfully develop the countermeasures we need. This approach shifts the risks off the taxpayer and onto the industry for the inevitable research failures. The government pays only for success, not process.

Furthermore, this breakthrough research won't be wasted if there is no bioterror attack. We desperately need to develop new antibiotics to replace those for which resistance is emerging. Even if no bioterror attack ever occurs, the work of the biotech industry could make significant progress toward finding cures for infectious diseases that are ravaging millions of people

Our bill complements the Administration's Project Bioshield. Project BioShield follows our lead by setting the terms in advance for government markets – our concept. It would give bio-pharmacological companies reliable commitments regarding the market they will tap if they risk their own capital to develop countermeasures. In all likelihood, Project Bioshield would result in the development of some new Bioterror antidotes. We

believe Congress should pass Project BioShield immediately. It's a step in the right direction.

We believe that more can and should be done to provide additional incentives to help infuse the biodefense industry with the talent and capital necessary to give us all the bioterror medicines we need. Bioterror is an evolving threat that could, over time, require development of dozens, perhaps hundreds, of medical countermeasures. The Lieberman-Hatch bill would pave the way for industry involvement sufficient to meet the potential need.

We will know that we've established a biodefense industry when hundreds of millions of dollars in company and investor capital are available to fund countermeasure research, and investors see a reasonable opportunity to profit to the same degree they do on investments in other biomedical research.

We urge Congress to move expeditiously on the President's BioShield bill and then take up BioShield II, a bill we'll introduce once BioShield is enacted. It will be based on our own bipartisan legislation. That combination will advance the process of building a biodefense industry to protect us from future biological attacks.

In the long run, we may face no greater threat than a bioterror pathogen. Now is the time to come together to ensure that we are ready with the medical countermeasures – and the public health infrastructure – to prevent panic and minimize what could otherwise be massive loss of life. We will continue to work with President Bush, our colleagues in the Congress, and other interested parties on this important matter.

Chronology: Incentives for Research to Develop Countermeasures to Bioterror Pathogens

Summer 2000 — Defense Science Board finds that we have only 1 of the 57 bioterror countermeasures we most need

October 5, 2001 — Bob Stevens, a photo editor at American Media in Boca Reton, Florida, dies of inhalation anthrax.

October 7, 2001—U.S. Centers for Disease Control and Prevention (CDC) reported that investigators had detected evidence that the deadly anthrax bacterium was present in the building where Stevens had worked.

October 12, 2001 — NBC employee in New York exposed to anthrax.

October 15, 2001 — Anthrax laced letter opened in Senator Daschle's Office in the Hart Senate Office Building. ABC News finds anthrax in its offices in New York.

October 18, 2001 — CBS news finds anthrax in its offices in New York.

October 19, 2001 — New York Post finds anthrax at its offices in New York.

October 21-22, 2001 — Washington, D.C. area postal workers are diagnosed with inhalation anthrax after two others had died.

October 31, 2001 — New York supply clerk Kathy Nguyen dies of inhalation anthrax.

November 21, 2001 — Connecticut woman, Dottie Lungren, dies of inhalation anthrax.

December 4, 2001 — Senator Lieberman introduces S. 1764, a comprehensive set of incentives for research on countermeasures for bioterror agents

October 15, 2002 — First Anniversary of Daschle Office anthrax attack – no Administration proposal submitted to the Congress

October 17, 2002 — Senators Lieberman and Hatch introduce S. 3148, a refined version of S. 1764

January 29, 2003 — President Bush in his State of the Union Address calls for Congress to enact Project BioShield; it is modeled on one of twelve key provisions in S. 3148 (guaranteed procurement incentives)

March 19, 2003 — Senators Lieberman and Hatch introduce S. 666, a further refined version of S. 3148

March 25, 2003 — Senator Gregg introduces S. 15 -- the text of BioShield as submitted by the President

May 15, 2003 — H.R. 2122 introduced -- the House version of BioShield

June 10-July 18, 2003 — Three House Committees report H.R. 2122

July 16, 2003 — House passes H.R. 2122

September 2, 2003 — Senator Gregg introduces S. 1504 -- legislation similar to S. 15

October 15, 2003 — Second Anniversary of the Daschle Office anthrax attack

November 24, 2003 — President signs Department of Defense Authorization Act, H.R. 1588, Public Law 108-136, which contains a version of BioShield

May 19, 2004 — Senate passes S. 15 on a vote of 99-0 with an amendment (a complete substitute) based on the House-passed bill. Amendment No. 3178. S. 15 is now pending in the House.

July 14, 2004 — House passes S. 15 414-2. It goes to the President for his signature.

July 21, 2004 — President signs BioShield into law as Public Law 108-276

Senators Lieberman and Hatch have announced that they will introduce BioShield II, which will re-propose eleven incentives from S. 1764, S. 3148, and S. 666 that were not included in BioShield.

BIOLOGICAL, CHEMICAL AND RADIOLOGICAL WEAPONS COUNTERMEASURES RESEARCH ACT OF 2003, S. 666

Senators Lieberman and Hatch

The legislation[22] proposes incentives that will enable biotechnology and pharmaceutical companies to take the initiative -- for good business reasons -- to conduct research to develop countermeasures, including diagnostics, therapeutics, and vaccines, to treat those who might be exposed to or infected by biological, chemical or radiological agents and materials in a terror attack.

The premise of this legislation is that direct government funding of this research is likely to be much more expensive and risky to the government and less likely to produce the countermeasures we need to defend America. Shifting some of the expense and risk of this research to entrepreneurial private sector firms is likely to be less expensive and much more likely to produce the countermeasures we need to protect ourselves in the event of an attack.

For biotechnology companies, incentives for capital formation are needed because most such companies have no approved products or revenue from product sales to fund research. They rely on investors and equity capital markets to fund the research. These companies must focus on research that will lead to product sales and revenue and end their dependence on investor capital. When they are able to form the capital to fund research, biotech companies tend to be innovative and nimble and focused on the intractable diseases for which no effective medical treatments are available. Special research credits for pharmaceutical companies are also needed.

For both biotech and pharmaceutical companies, there is no established or predictable market for these countermeasures. Investors and companies are justifiably reluctant to fund this research, which will present technical challenges similar in complexity to development of effective treatments for AIDS. Investors and companies need assurances that research on countermeasures has the potential to provide a rate of return commensurate with the risk, complexity and cost of the research, a rate of return comparable to that which may arise from a treatment for cancer, MS, Cystic Fibrosis and other major diseases or from other investments.

President Bush's BioShield initiative is designed to establish and predictable market for these countermeasures. This legislation provides a template for implementation of BioShield and supplements it with additional incentives to ensure that the industry is enthusiastically engaged in this vital research.

The legislation provides tax incentives to enable companies to form capital to conduct the research and tax credits usable by larger companies with tax liability with

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[22] The legislation was originally introduced by Senator Lieberman on December 4, 2001 as S. 1764. It was reintroduced by Senators Lieberman and Hatch on October 17, 2002, as S. 3148.

respect to which to claim the credits. It provides a guaranteed and pre-determined market for the countermeasures and special intellectual property protections to serve as a substitute for a market. Finally, it establishes liability protections for the countermeasures that are developed.

Section 3 of the legislation is drafted as an amendment to the Homeland Security Act of 2002 (HSA)(P.L. 107-296). Section 2 sets forth findings and sections 4-9 are drafted as amendments to other statutes.

1. Setting Research Priorities (Section 1811 of HSA): The Department of Homeland Security sets the countermeasure research priorities in advance. It focuses the priorities on threats for which countermeasures are needed, and with regard to which the incentives make it "more likely" that the private sector will conduct the research to develop countermeasures. It is required to consider the status of existing research, the availability of non-countermeasure markets for the research, and the most effective strategy for ensuring that the research goes forward. The Department then provides information to potential manufacturers of these countermeasures in sufficient detail to permit them to conduct the research and determine when they have developed the needed countermeasure. The Department is responsible for determining when a manufacturer has, in fact, successfully developed the needed countermeasure.

2. Registration of Companies (Section 1812 of HSA): Biotechnology and pharmaceutical companies register with the Department to become eligible for the incentives in the legislation. They are obligated to provide reports to the Department as requested and be open to inspections. The Department certifies which companies are eligible for the incentives.

Once a company is certified as eligible for the incentives, it becomes eligible for the tax incentives for capital formation, and if it successfully develops a countermeasure that meets the specifications of the Department, it becomes eligible for the procurement, patent, and liability provisions.

3. Diagnostics (Sections 1813 and 1814 of HSA): The incentives apply to development of detection systems and diagnostics, as well as drugs, vaccines and other needed countermeasures.

4. Research Tools (Section 1815 of HSA): A company is also eligible for certification for the tax and patent provisions if it seeks to develop a research tool that will make it possible to quickly develop a countermeasure to a previously unknown agent or toxin, or an agent or toxin not targeted by the Department for research.

5. Capital Formation for Countermeasures Research (Section 1821 of HSA; also section 4 of the legislation): The legislation provides that a company seeking to fund research is eligible to elect from among four tax incentives. The companies are eligible to:

(a). Establish an R&D Limited Partnership to conduct the research. The partnership passes through all business deductions and credits to the partners.
(b). Issue a special class of stock for the entity to conduct the research. The investors would be entitled to a zero capital gains tax rate on any gains realized on the stock.
(c). Receive a special tax credit to help fund the research.
(d). Receive a special tax credit for research conducted at a non-profit and academic research institution.

A company must elect only one of these incentives and, if it elects one of these incentives, it is then not eligible to receive benefits under the Orphan Drug Act. The legislation includes amendments (Section 9 of this legislation) to the Orphan Drug Act championed by Senators Hatch, Kennedy and Jeffords (S. 1341). The amendments make the Credit available from the date of the application for Orphan Drug status, not the date the application is approved as provided under current law.

6. Countermeasure Purchase Fund (Section 1822 of HSA): The legislation provides that a company that successfully develops a countermeasure -- through FDA approval -- is eligible to sell the product to the Federal government at a pre-established price and in a pre-determined amount. The company is given notice of the terms of the sale before it commences the research.

7. Intellectual Property Incentives (Section 1823 of HSA; also section 5 of this legislation): The legislation provides that a company that successfully develops a countermeasure is eligible to elect one of two patent incentives. The two alternatives are as follows:

(a). The company is eligible to receive a patent for its invention with a term as long as the term of the patent when it was issued by the Patent and Trademark Office, without any erosion due to delays in the FDA approval process. This alternative is available to any company that successfully develops a countermeasure irrespective of its paid-in capital.
(b). The company is eligible to extend the term of any patent owned by the company for two years. The patent may not be one that is acquired by the company from a third party. This is included as a capital formation incentive for small biotechnology companies with less than $750 million in paid-in capital, or, at the discretion of the Department of Homeland Security, to any firm that successfully develops a countermeasure.

In addition, a company that successfully develops a countermeasure is eligible for a 10-year period of market exclusivity on the countermeasure.

8. Liability Protections (Section 1824 of HAS; also Section 10 of the legislation): The legislation provides for protections against liability for the company that successfully develops a countermeasure.

9. Accelerated Approval of Countermeasure (Section 1831 of HSA): The countermeasures are considered for approval by the FDA on a "fast track" basis.

10. Special Approval Standards (Section 6 of this legislation: The countermeasures may be approved in the absence of human clinical trails if such trails are impractical or unethical.

11. Limited Antitrust Exemption (Section 7 of this legislation): Companies are granted a limited exemption from the antitrust laws as they seek to expedite research on countermeasures.

12. Biologics Manufacturing Capacity and Efficiency (Section 1832 and 1833 of HSA; and section 8 of this legislation): Special incentives are incorporated to ensure that manufacturing capacity is available for countermeasures.

13. Strengthening of Biomedical Research Infrastructure (Section 1834 and 1835 of HSA): Authorizes appropriations for grants to construct specialized biosafety containment facilities where biological agents can be handled safely without exposing researchers and the public to danger (Section 216). Also reauthorizes a successful NIH-industry partnership challenge grants to promote joint ventures between NIH and its grantees and for-profit biotechnology, pharmaceutical and medical device industries with regard to the development of countermeasures and research tools (Section 217).

14.Annual Report (Section 1841 of HSA): The Department is required to prepare for the Congress an annual report on the implementation of these incentives.

15. International Conference (Section 1842 of HSA): The Department is required to organize an annual international conference on countermeasure research.

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BioPharma vs. Defense Contractor Operating Margins

The operating margin for successful biopharma companies is 2.76 to 3.74 times as great as the operating margins for major defense contractors. This means that the defense contractor model will not work to engage biopharma companies in developing medical countermeasures for bioterror agents. Whether the successful bipharma companies are "too profitable" is a separate issue. The issue addressed here is the operating margin that successful biopharma companies seek and expect as they assess lines of research to undertake. If the operating margin for biodefense research is drastically less than the operating margin for non-biodefense research, it is not likely that these companies will choose to undertake biodefense research.

The operating margin for the major defense contractors listed below was 8.5% in 2001 and 9.5% in 2002.

Defense Contractor	Operating Margins 2001	2002
Boeing		
company	6.7%	7.2%
military	10.8%	11.8%
General Dynamics		
company	12.9%	11.4%
marine systems	8.6%	7.9%
info systems	9.3%	11.8%
combat systems	10.8%	11.1%
L-3 Communications	4.4%	9.9%
Lockheed Margin		
company	3.7%	8.5%
systems integration	9.3%	9.9%
aeronautical systems	7.8%	6.9%
Northrop Grumman		
company	7.4%	8.1%
electronic systems	7.6%	8.1%
ships	1.0%	6.5%
integrated systems	8.6%	10.1%
Ratheon		
company	12.0%	11.4%
electronic systems	13.7%	13.5%
C3I systems	10.5%	10.0%
Rockwell Collins		
company	16.3%	14.7%
Teledyne		
Company	4.9%	5.6%
Average	**8.5%**	**9.6%**

The operating margin for the successful biotechnology companies listed below was 31.8% in 2001 and 28% in 2002. This operating margin is 3.74 times and 2.91 times as great for 2001 and 2002 respectively as the operating margin for the defense contractors listed above.

U.S. Biotechnology	Operating Margins	
	2001	2002
Amgen	44.2%	41.8%
Biogen	34.5%	26.3%
Cephalon		25.9%
Chiron	19.5%	24.3%
Genentech	22.7%	24%
Genzyme	22.3%	21.8%
Gilead		17.4%
IDEC	48.1%	52.9%
MedImmune	31.1%	17.2%
Average	31.8%	28.0%

The operating margin for the successful pharmaceutical companies listed below was 29.5% in 2001 and 26.5% in 2002. This operating margin is 3.47 and 2.76 times as great for 2001 and 2002 respectively as the operating margin for the defense contractors listed above.

U.S. Pharma	Operating Margins	
	2001	2002
Bristol-Myers	33.2%	21.9%
Eli Lilly	32.3%	29.5%
Merck	21.0%	19.0%
Pfizer	34.2%	36.1%
Schering Plough	30.0%	27.7%
Wyeth	26.1%	24.5%
Average	29.5%	26.5%

Operating margin is profit before tax. The operating margin for the defense contractors has been adjusted for good will. Operating margin is calculated by dividing a company's operating profit by net sales. It is also known as operating profit margin or net profit margin. Operating profit it typically assessed before taking into account interest and taxes.

Compiled from publicly available information with assistance from Michael King, Banc of America Securities LLC.

Interview—Serguei Popov
Journal of Homeland Security (November 13, 2000)

Serguei Popov is a former scientist in the Russian biological warfare program. After obtaining a degree in biochemistry, he served as a division head in Vector and Obolensk, branches of the Soviet program dedicated to developing genetically enhanced bioweapons. His position allowed him to expand his research into the fields of molecular biology and microbiology. Dr. Popov worked at Vector from 1976 to 1986, then at Obolensk until 1992, when he defected to Britain and later traveled to the United States. He now works for Hadron, Inc., in microbiology and pharmacology.

Homeland Defense: *How did you first become involved in the Soviets' biological warfare program?*

Serguei Popov: I found work by speaking to Lev Sandakchiev, who later became in charge of Vector Institute. Lev wasn't my friend but I knew him very well. My wife was a student of his at that time, so there was a close connection. Of course, I had no knowledge of what specific programs they had decided to run, but in 1975, Sandakchiev wanted me very much to join his institute. And shortly thereafter I became a scientist for him at Vector.

Homeland Defense: *What were some of your earliest projects at Vector?*

Serguei Popov: With my background in biochemistry and nucleic acid chemistry, I primarily studied DNA. At that time, it was not a very advanced science, but it was exciting and we tried to create artificial DNA fragments and artificial genes. That was my goal, actually, for the next several years, to make artificial genes. I eventually became the head of a department, with about 50-60 people working with me, half of whom were researchers.

Our approaches were straightforward, using mainly chemical synthesis. It was certainly easier than other available procedures. And chemical synthesis was attractive because it promised to do whatever we wanted. And of course Sandakchiev was interested. That same year, 1976, I became a department head—a department whose whole purpose was to learn how to design artificial genes.

Homeland Defense: *Could you describe the different levels of security in your program?*

Serguei Popov: Early on, I was already at security level three, but there were at least four levels of security. At level one, the explanation, called "an open legend," was that there was no biological weapons program at all. The work at the institute was completely academic and open. At level two, there was "a closed legend" explaining that there was a strictly defensive weapons program. At the third level, a particular person was provided with a description of some programs there were and what were the true purposes of these programs. But even this wasn't the complete truth. The real truth was at level four, which I viewed only briefly much later on. I read these types of documents on only one occasion.

Level number four described the purpose of specific programs and their interconnections. I read some of them, but I didn't know the whole picture. And I believe that below level four, there was yet another level with a full description of all the bioweapons programs. That was for the government. I didn't have that big picture. I think that Ken Alibek had that big vision. I have just fragments of that vision.

Homeland Defense: *When did you realize you were involved in biological weapons production?*

Serguei Popov: It happened both gradually and immediately. With a program like Vector, you know something is going on, but no one tells you what you are going to do, or what the precise purpose of your program is. People get involved step by step, in such a way that there is no way back. You sign papers, and you commit yourself.

Homeland Defense: *How did the conditions at Vector compare to the working conditions in Biopreparat?*

Serguei Popov: There were subtle differences between the Siberian institution of Vector and the other institutions of Biopreparat. Lev Sandakchiev was a pure scientist and had never been involved previously in biological weapons programs. So, the approach of Vector was the scientific approach. In contrast, the people who organized the Obolensk Institute had experience in biological weapons. The whole mentality was different. In Siberia, there was more a sense of freedom, adventure, excitement, and a sense of discovery. The other place, as I understand it, was much more depressing.

Homeland Defense: *At that time, did they tell you the United States was involved in offensive biological weapons?*

Serguei Popov: Yes, they did. They always did. And there was no way to explore that point of view, even if we believed otherwise. It was an official statement and no one doubted it.

Homeland Defense: *Did they also tell you the United States was working on genetically enhanced weapons?*

Serguei Popov: That wasn't difficult to believe either. The United States is the biggest country, with some of the best scientists, you know. So I had no doubts.

Homeland Defense: *So when did you realize the U.S. was out of the biological warfare program?*

Serguei Popov: Not until I came to this country. I knew what was written about the U.S. program. But I had a suspicion that nothing was happening in this country when I visited England in 1979. When I visited England, it didn't take long to pick it up.

Homeland Defense: *Dr. Popov, this interview in generally targeted for the benefit of two groups: individuals with strong scientific background, and at the opposite end of the spectrum, policy makers with little background in the sciences but strong interests in the subject matter. But there is likely one question in particular that both sides could agree on in terms of importance. In our discussions with Dr. Alibek, agents like plague, anthrax and smallpox all sounded like very effective weapons.*

Serguei Popov: Oh, they are.

Homeland Defense: *What then was the purpose of taking this next step, which was really leading-edge science? Why genetic engineering?*

Serguei Popov: The answer changed over time. Originally, the Soviet military wanted Vector and Obolensk to produce genetically engineered weapons because they wanted classical agents with new properties like higher pathogenicity and unusual symptoms. And ultimately, we did develop improved classical weapons, with new, unusual properties and resistance to antibiotics.

But it proved to be an illogical way to construct a weapon. There was a belief that new weapons, completely new weapons, without known protection and with new properties, could be superior. The classical agents were there, and they were effective, but initially the military wanted even more effective [ones].

Homeland Defense: *Now, Dr. Alibek told us last month about how Biopreparat developed plague that was resistant to our ten most common antibiotics. They couldn't find a strain of plague resistant to ten, so they took one strain, made it resistant to five, and another to another five. Were you just looking for more effective ways to achieve the same result?*

Serguei Popov: Not exactly. When we talk about the whole program of genetically engineered weapons, it was a combination of several projects. For example, projects like "Bonfire" were specifically aimed at developing antibiotically resistant strains.
But there was a much bigger program, called "Factor." It was a program to create strains with the ability to produce certain biologically active substances as new pathogenic factors. It was not about an improvement of what was generally known. But the final goal of Factor was to create strains with completely new properties.

Homeland Defense: *Did Factor also work with the classical agents?*

Serguei Popov: Yes. The initial vision was that the old classical biological weapons would acquire new, unusual properties so that, for example, prophylaxis would be difficult. Project goals included high virulence, high stability, and surprising new outcomes for the disease in order to confuse treatment. To achieve those goals, there were several directions. The first was to express short biologically active peptides. Then there was an attempt to introduce toxin genes into those strains. The toxin genes could be short peptide toxins or they could be proteins.

Homeland Defense: *In follow-up, you commented on the plague issue, that somehow there was recent success in achieving the properties. Is that what you're suggesting?*

Serguei Popov: Yes. I know at least two examples of plague and smallpox strains which acquired new properties.

Homeland Defense: *And what would those properties be?*

Serguei Popov: A gene responsible for hemorrhage formation was included in one viral strain and diphtheria toxin gene in another bacterial strain. Later, the Obolensk Institute published their results on anthrax with hemolysin gene. That was the third example. But again, in [the] case of diphtheria toxin, we were more interested in the outcome. The idea was that the vaccine directed against plague would not be effective. When we talked about those problems, there is no clear way to achieve those goals. That's why the programs constantly changed. The final purpose was the same but the way to achieve success varied.

Homeland Defense: *For the benefit of the non-scientific audience, could you describe what a peptide basically is?*

Serguei Popov: A peptide is a short protein fragment. Peptides are of the same origin and display properties of proteins. But peptides are more direct in their action and properties. They may target specific functions. We have an example of small peptides like endorphins or enkephalins. Those peptides are approximately 30 amino acids long, and it is about 10 to 20 times [fewer] amino acids than in an average protein. The peptides can interact with a receptor, and they could be produced in a biological way. It's difficult to produce morphine or other drugs through genetic means. But endorphin peptides have similar properties. In the case of peptides, you make a very small DNA chain that codes for the peptide, and you introduce that gene into the genome of any agent. That's, in general, all you need.
Small peptides that are neuro-active were capable of changing behavior. Some peptides also created changes of behavior and could have other activities, because they were multifunctional peptides. One example of this was vasopressin, which affects blood pressure. Some peptides were toxins, while others offered a completely new approach for causing autoimmune diseases.

Homeland Defense: *What do you think about press reports which suggest it's possible to take the toxin from cobra venom and splice it into strains of influenza?*

Serguei Popov: Those are all an exaggeration, but the idea is correct. I would doubt that cobra venom would be good for biological expression. Toxins must meet numerous specific requirements. But the simplest is that they should be easy to reproduce in biologically active ways. Many toxins are also big molecules, requiring energy and specific biological machinery to build and deliver them to their specific targets. If you

consider the simplest toxin, it should be short, it should not be sensitive to the environment, and it should be stable when created inside the body.

Homeland Defense: *Did you have any success in creating these?*

Serguei Popov: Well, essentially, yes. There are several toxins which are very effective, like peptide toxins from cone snails (conotoxins). However, there were some problems. One of them was that those toxins required two specific cystine bridges. Without those bridges they weren't biologically active, and that was a complication.

Homeland Defense: *But you successfully produced those toxins?*

Serguei Popov: Finally, yes. The work on inserting them into smallpox virus continued till the program was terminated.

Homeland Defense: *Was it your goal to produce the toxins in quantities sufficient by themselves, or was it always part of your plan for one organism to produce the toxins inside the host?*

Serguei Popov: The final goal of Factor was to create microorganisms that produce these toxins inside the host. But there was another program that dealt directly with toxins themselves. It was closely linked to Factor because when we studied the action of toxins engineered into microbes, we had to know their behavior, meaning we needed them in control experiments. The goal of genetically engineering the weapons was to create strains of microorganism producing toxins, such as viruses coding for toxins and ultimately producing toxins.

Homeland Defense: *Were you successful? You were talking about genetically engineering strains of the classic biological weapons, so that they were more effective, had different properties, and presented themselves in new, challenging ways. But did you ultimately produce an anthrax or smallpox agent with new properties?*

Serguei Popov: Yes; for example, plague with diphtheria toxin has been produced. But the whole program was a difficult task. Some approaches proved to be more successful than others. One tactic, immune mimicry, was to induce an immune response against myelin (found in the body's nervous system). Because the cloned myelin protein (or its fragment) would be very close in structure to the body's, host responses against the infection would be directed against the body's own myelin. As a general principle it's been discussed for many years, but it's a very difficult practical task to pull off. Damaged myelin interferes with the transmission from the brain to the peripheral nerves. Most likely its destruction by a microbial agent would induce paralysis and death.
For example: You get the flu, and then you get a complication from the flu. In that case, the immune system, which struggled with flu virus, could target your body as well as flu. When your body tries to heal itself, it actually does the reverse.
In Obolensk, we did extensive experimentation with different bacteria carrying a myelin gene. We finally found that an agent called Legionella created very strong immunological

responses. The myelin peptide it produced was very immunogenic because the immune system was activated by the infectious process. That's what resulted in paralysis and death of infected experimental animals. And what is important as well, a lethal dose was much lower, only a few Legionella cells.

Homeland Defense: *Were you able to do that in animal models, like primates?*

Serguei Popov: No, just guinea pigs. We were initially ordered to do it, and we did not expect any technical difficulty, but the program had been abruptly stopped at the level of primates.

Homeland Defense: *And how long would it take before the target was affected?*

Serguei Popov: Essentially, it's two weeks.

Homeland Defense: *And there would be no symptoms before that?*

Serguei Popov: No, there wouldn't, and there would be no agent in your body. It will be completely clear.

Homeland Defense: *Doctor Popov, this sounds like a topic that very few people in the areas of biological warfare and homeland defense have discussed. It also sounds like a very challenging weapon to guard against. Could you offer any additional explanations on this subject?*

Serguei Popov: Certainly. In general, there is a basic technique to make a viral or bacterial genome easier to manipulate genetically. First you take a gene of interest and you put it in a suitable biological vehicle, often called a vector. Here the gene can be changed, and new properties can be added. More importantly, the vector could be introduced into a bacterial strain, so that the bacteria will carry it, and will acquire the properties to produce the substance the gene codes for. Usually, the bacterial host is harmless, but it can be pathogenic. The gene product can be pathogenic as well. In the above case of the myelin peptide, [the] immune system eliminates the bacteria that produced it, but the peptide triggers a slow destructive immune response. And you are right when you say people in biodefense have never considered this approach.
Let me provide you with another example of a new bioweapon idea, which was under development when I left Russia. Imagine plague carrying a whole copy of a virus. You would expect that people infected with genetically engineered strains of plague would be treated for plague. But the antibiotic treatment would actually make the patient worse because of the antibiotic-induced release of the virus from its copy. A virus infection on top of a bacterial infection may be a situation you will never be able to properly deal with.

Homeland Defense: *So you don't have the virus until you kill the bacteria?*

Serguei Popov: No, you don't.

Homeland Defense: *In the exercise we did in May, called "Topoff," in Denver, we did the simulation of a plague attack, and they chose plague because treatment, in theory, is simple. You just need to provide people with antibiotics. But in your scenario, it wouldn't matter. No matter how effective we are at controlling it, the more antibiotics you pass out, the more viruses you release?*

Serguei Popov: Exactly. Each disease has completely different symptoms and incubation periods, which means treated people will appear healthy and think they are fine. But the treated people are still sick. They simply don't know it. And a new viral disease can appear after a few days in cases of recombinant plague, or two or three weeks in case of recombinant Legionella. People will experience paralysis, and their central nervous system will cease to function.

Homeland Defense: *And how long does it take for this paralysis to take effect?*

Serguei Popov: It's difficult to say, but the disease itself in animals is quite fast (a few days).

Homeland Defense: *Some of the peptides you've mentioned are extremely novel. But in looking at some of your viral agents, was it more in your interest to create new properties, or to perpetuate existing systems?*

Serguei Popov: Initially, the purpose was to bring new properties to existing strains. But the whole program shifted development in the 1980s into new strains. We struggled with the problem of small peptides creating new properties, putting them into active strains. We began to ask ourselves, "Why should we insert peptides into classical strains when we could put them in new strains with new properties, and it could become a weapon even more difficult to deal with or cure?" So the whole plan of the program was shifted to making new virulent strains. In this area, I was relatively successful in making autoimmune peptides effective.

Homeland Defense: *Was your specialty in bacterial vectors, or did you look at viral vectors?*

Serguei Popov: I studied viral vectors originally. But after I was transferred to the Obolensk Institution, I worked on bacterial vectors as well.

Homeland Defense: *You stated earlier that one of the goals of Project Bonfire was vaccine resistance. How much success did your program have in developing a strain of anthrax resistant to vaccinations?*

Serguei Popov: I heard a story in 1986 about developing an anthrax resistant strain expressing hemolysin, but [at] that time it wasn't considered a very productive way of doing vaccine resistance against anthrax, and that was in place a long time ago. I did not think they would find anything very exciting about this. Surprisingly, it finally worked.

Homeland Defense: *Out of curiosity, was tularemia an interest of your program?*

Serguei Popov: Well it was, but it was considered an old workhorse, an old vehicle. In terms of genetic engineering with tularemia, there was little activity.

Homeland Defense: *How about mycoplasm?*

Serguei Popov: We didn't try that. I know that they looked at it, but that was in a different institute.

Homeland Defense: *Did your program share work with allied countries, or was it only with Russian scientists?*

Serguei Popov: No, my program only employed Russians. And there was no change in this policy up until 1992, when I left Russia.

Homeland Defense: *So you did no work except for biological weapons work?*

Serguei Popov: Yes, but it was not easy to distinguish between pure science and military science applications. In a way, everything had military usage. Anything considered "pure science" was questionable. Take an example of a recombinant interferon project I was in charge of at Vector. It was believed to be a potent antiviral drug for troops' protection.

Homeland Defense: *How much control did the Soviet Union have over your life? Was your travel restricted?*

Serguei Popov: Traveling abroad was completely impossible. I managed it once and that was it. But travel inside the country was restricted in terms of procedures. You had to be back in the lab by certain times. That type of thing took place frequently.

Homeland Defense: *When you began this in the 1970s and 1980s, you were involved in what we would call leading-edge technologies. Only Russia, the United States, and maybe a few other countries like the United Kingdom could reasonably succeed in this area. Because of the biotechnology revolution, do you think this type of research is continuing today in other countries like Iran, China, India, or North Korea?*

Serguei Popov: I think the answer to your question is: no doubt. But the knowledge is not there, I hope. Creating biological agents is not only technology and procedures. But the most important thing is what to do, and how to achieve success.

Homeland Defense: *Do you believe it's possible some of these countries have recruited former colleagues of yours to work for them in this area?*

Serguei Popov: Oh, I'm pretty sure they did.

Homeland Defense: *And how many people worked in your program at Vector, at your level and with your expertise?*
Serguei Popov: It's hard to estimate. I know there were several institutions, with several labs in each. There were probably a few thousand researchers. But at my level, there were maybe several dozen, as of 1992.

Homeland Defense: *Russia has ostensibly been opened to travel, but we assume someone with your skills would probably have been discouraged from leaving. Can you tell us about how you came out?*

Serguei Popov: Well, of course it wasn't the straight way. When I recognized that everything was collapsing and the KGB was having problems maintaining control, I decided it was a good time to get out. My problem, however, was that I had no money at all, not even to buy food. My only connection outside Russia was in England. I had visited England once in 1979 and I had some good friends over there in the scientific community. In fact, that's why [the] Soviets didn't let me join the communist party in the Soviet Union.
So I wrote those friends by sending them email and faxes. Finally, they found some money for me to conduct research, but still didn't have money for tickets. At the time, I only had four dollars in my pocket.
But the Royal Society promised to pay me in England. So I negotiated a short-term pass to England, and the KGB agreed to let me go. They may have agreed because they wanted the money that would come from the science I promised them. So they let me go. I just didn't go back.

Homeland Defense: *Do you feel like you've been threatened since then? Did they follow you?*

Serguei Popov: They followed my wife. When I left my home, I had to leave my family and my children in the Soviet Union for about a year. She knew I was going. But that was the only way to earn money, so that we could purchase their passports.

Homeland Defense: *When you left, were you debriefed by British or American intelligence services?*

Serguei Popov: Nobody was interested. Not a single person. Only much later, in Dallas, Texas, was I debriefed.

Homeland Defense: *So where have you been working and what have you been doing since you left Russia in 1992?*

Serguei Popov: Well, first I came to England. The Medical Research Council arranged for me to study molecular biology in Cambridge, and I studied HIV virus for six months there. Then I traveled to Dallas, and I researched microbiology and pharmacology. And today I work for Hadron.

Homeland Defense: *So to the best of your knowledge, the genetically engineered agents were not weaponized by the military?*

Serguei Popov: That is correct, but with a few exceptions. I think plague with diphtheria toxin was weaponized. That's my impression. The antibiotic-resistant strains of plague and anthrax were also weaponized. But as far as the Factor program is concerned, not very much was weaponized. I also know that hemorrhage gene was introduced into smallpox virus; I don't know the final results.

Homeland Defense: *Did you work on the smallpox virus yourself?*

Serguei Popov: Yes. But that project belonged primarily to another person. And I don't know if they decided to continue this work.

Homeland Defense: *There have been rumors of combining smallpox and Ebola after some fashion. Some have suggested making an agent as contagious as smallpox and as deadly [as] Ebola. Is such a thing possible?*

Serguei Popov: This idea could be accomplished on a genetically defined level, or by simply combining both. The physical combination was the subject of discussion. But not everybody liked it because of the difficulties involved.

Homeland Defense: *Did you hear about this in Russia or after you came here?*

Serguei Popov: From 1986 I heard some rumors on these types of agents. Both bacterial and viral combinations were discussed, but I was not included in these talks. To be honest, I had little interest in this area.

Homeland Defense: *You mentioned the development of "subtle agents," using biopeptides and bioregulators. Did Vector also work on similar agents that would affect people from a psychological perspective?*

Serguei Popov: Yes, endorphins, enkephalins, and other neuromodulating peptides. It has been discovered that personalities could be adjusted with these agents. For example, you could make people more aggressive. Or you could create feelings of insomnia, where people wanted to sleep, but would never feel tired.

Homeland Defense: *In your program, who decided where the work would go? Was it the military, the government, or the scientists?*

Serguei Popov: Factor was literally created overnight in a Moscow kitchen by some military officers, sometime around 1978. From that point on, it became an official program, but they always took feedback from scientists. They realized it was the perfect way to make new agents, which could be essentially undetectable, and furthermore could get around the biological weapons treaty. Many of the agents created by Factor would be very dangerous, but they would not be illegal.

Editor's note: *The Journal of Homeland Defense* disagrees with the Soviet claim that such activity was legal. The Biological and Toxin Weapons Convention prohibits any type of activity (development, production, or stockpiling) regarding the offensive use of biological or toxin weapons. Article I from the convention is provided at the end of the interview for the readers' perusal.

Homeland Defense: *You've mentioned quite a few unsettling agents in today's discussion. But we want to be clear on this subject: were any of these agents weaponized in mass quantities?*

Serguei Popov: No, they were not. We ceased this work around 1991, after funding was cut.

Homeland Defense: *What happened to the research related to these projects?*

Serguei Popov: Everything was archived and put into storage, and I believe it is still there.

Homeland Defense: *This information sounds sensitive, if not dangerous. Do you know if this data is currently secure?*

Serguei Popov: To the best of my knowledge the information is still safe.

Homeland Defense: *What about your former colleagues? Do you believe any of this work you've discussed is still going on?*

Serguei Popov: Yeah, I'm pretty sure. I don't have any direct evidence. But recently I've begun looking up what my former colleagues have published. All I found were a few lousy, lousy papers. This suggests they are currently working on something they cannot publish. And that's a good indication the program is still functioning.

Homeland Defense: *Those papers are just cover stories?*

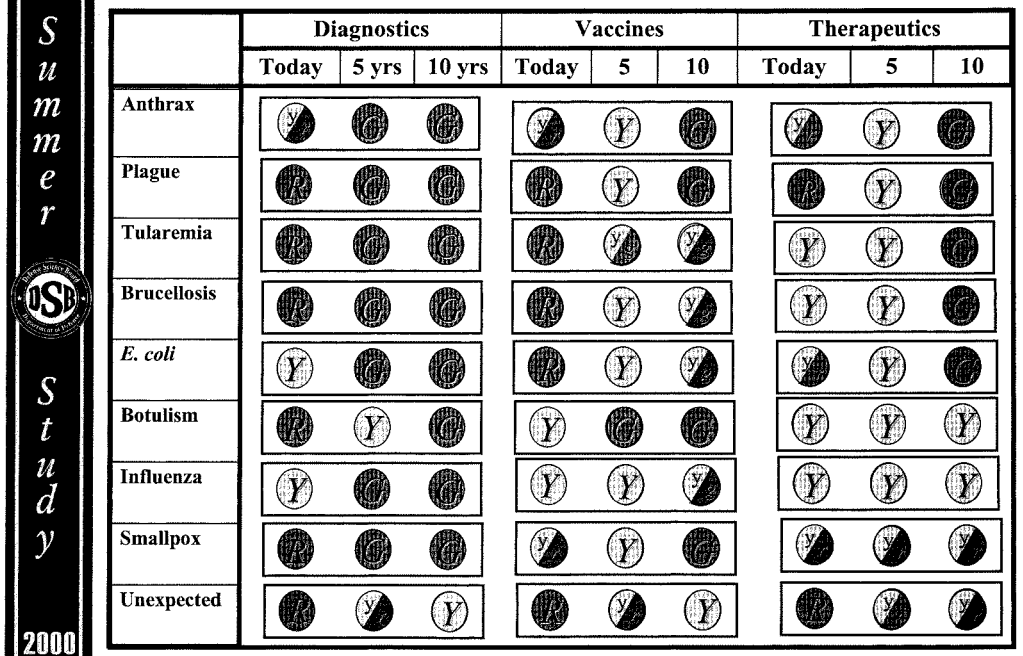
Serguei Popov: Yes. That's all they are allowed to publish.

Homeland Defense: *Finally, we should mention that this is your first public interview since you departed the Soviet Union. You said that the U.S. Intelligence Community debriefed you. Were the people who conducted this interview fully qualified to conduct your briefing? Did they have the proper scientific background to fully appreciate the nature of your previous work with the Soviet Union?*

Serguei Popov: No, they did not sound like scientists. However, I told them about the directions of my work in the Soviet Union. They were mainly concerned with the issues of possible terrorist attack using bioweapons.

2000 Summer Study 2000

The Projected Evolution of Diagnostics, Vaccines, and Therapeutics Against Major Bioagents with Strategic R&D and Supply Actions



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	Diagnostics			Vaccines			Therapeutics		
	T	5	10	T	5	10	T	5	10
Burkholderia mallei	R	G	G	R	R	Y	R	R	Y
B. pseudomallei	R	G	G	R	R	Y	R	R	Y
Chlamydia psittaci	Y	G	G	Y	Y	Y	G	G	G
Clostridium perfringens	R	G	G	R	R	R	R	Y	G
Salmonella	R	G	G	R	R	Y	Y	Y	y
Salmonella typhi	R	G	G	Y	G	G	Y	Y	y
Shigella	R	G	G	R	Y	G	Y	Y	y
Cholera	R	G	G	y	Y	G	Y	Y	y
Eastern Equine Encephalitis	R	G	G	Y	y	G	R	R	y
Venezuelan Equine Encephalitis	R	G	G	Y	y	G	R	R	y

2

Diagnostics	▪ Red	▪ Diagnosis in more than 24 hours ▪ Require confirmatory testing ▪ Must be symptomatic
	Yellow	Diagnosis 12-24 hrs May require confirmatory testing Some asymptomatic detection
	▪ Green	▪ Diagnosis <12 hrs ▪ No Confirmatory testing ▪ Asymptomatic detection
Vaccine	▪ Red	▪ Vaccine Not Available
	Yellow	Vaccine available. Production and/or use limitations
	▪ Green	▪ Generally available
Drugs	▪ Red	▪ No approved Treatment
	Yellow	Treatment available. Production and/or use limitations
	▪ Green	▪ Treatment available

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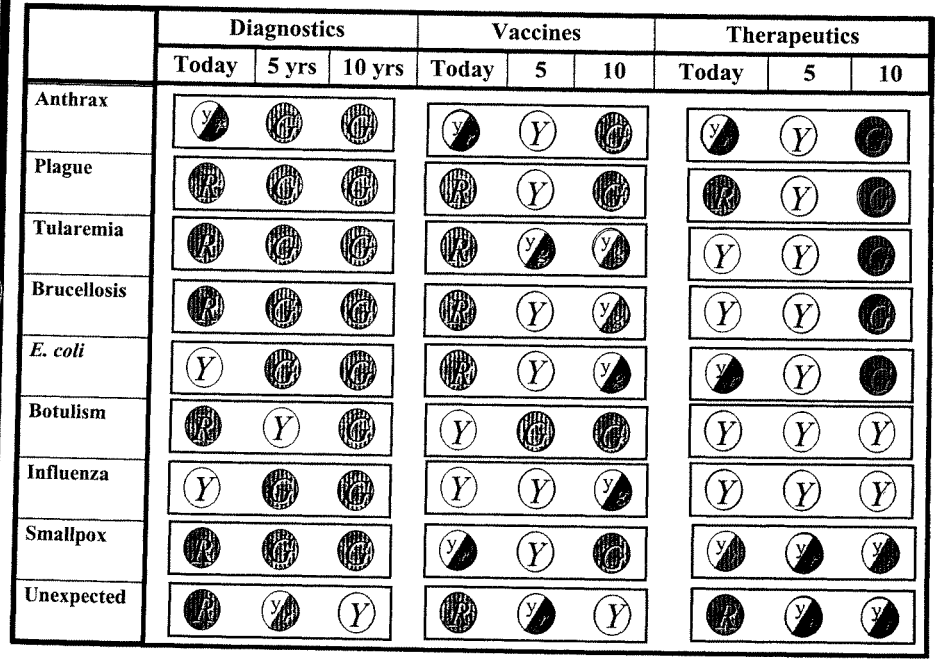

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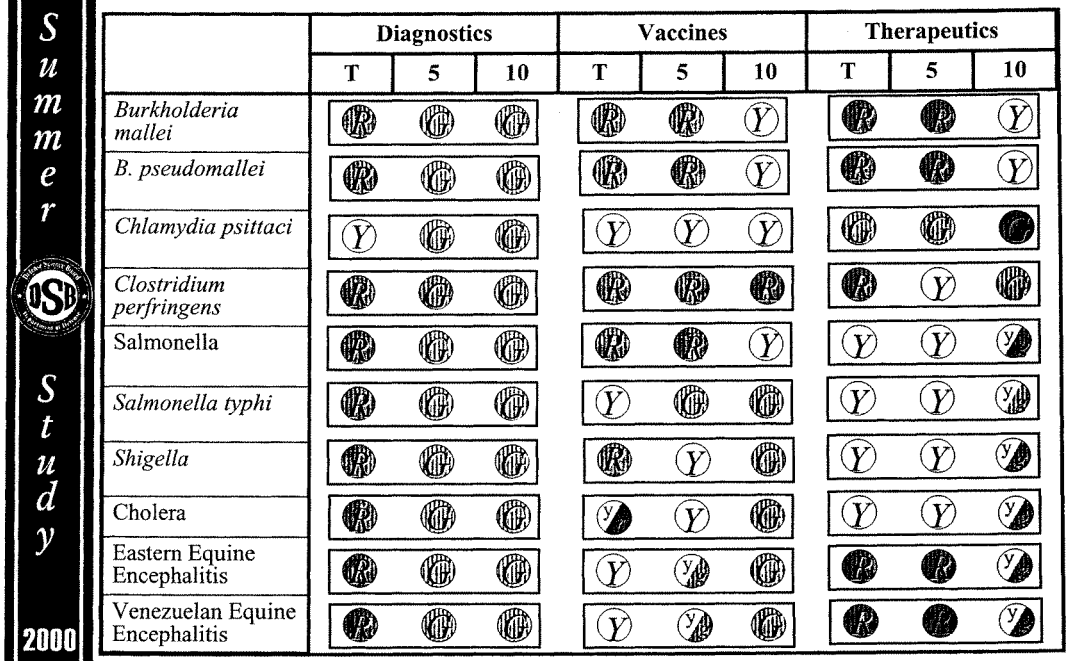

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Drugs	▪ Red	▪ No approved Treatment
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	▪ Green	▪ Treatment available

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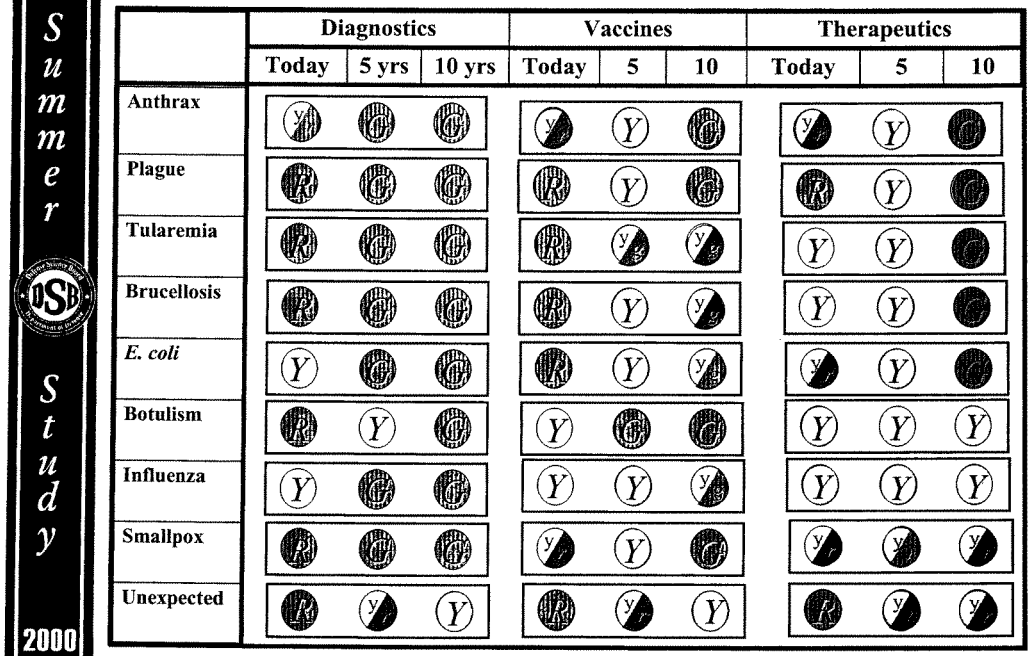

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	Diagnostics			Vaccines			Therapeutics		
	T	5	10	T	5	10	T	5	10
Burkholderia mallei									
B. pseudomallei									
Chlamydia psittaci									
Clostridium perfringens									
Salmonella									
Salmonella typhi									
Shigella									
Cholera									
Eastern Equine Encephalitis									
Venezuelan Equine Encephalitis									

Diagnostics	▪ Red	▪ Diagnosis in more than 24 hours ▪ Require confirmatory testing ▪ Must be symptomatic
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	Yellow	Vaccine available. Production and/or use limitations
	▪ Green	▪ Generally available
Drugs	▪ Red	▪ No approved Treatment
	Yellow	Treatment available. Production and/or use limitations
	▪ Green	▪ Treatment available

Statement of
JAMES G. RAFFERTY
HARKINS CUNNINGHAM LLP

Submitted to

THE COMMITTEE ON THE JUDICIARY AND
THE COMMITTEE ON HEALTH, EDUCATION, LABOR AND PENSIONS

UNITED STATES SENATE

October 6, 2004

"Bioshield II: Responding to an Ever Changing Threat"

I. INTRODUCTION

I am James G. Rafferty, Partner in the law firm of Harkins Cunningham LLP. I have 20 years' experience as a tax lawyer and have advised on tax matters a variety of private biotechnology companies, trade associations and other organizations. I am submitting this statement at the request of Senator Lieberman; and I do so on my own behalf and not as a representative of any organization.

I understand that the Committees are considering ways to promote private sector R&D on Bioterrorism countermeasures. You will hear today about possible "structural" changes -- from improved intellectual property protection and limitations on product and antitrust liabilities to guaranteed purchase arrangements -- which might create a more favorable overall climate for such research. My statement will focus on the range of tax policy options available to provide economic incentives for such research, particularly as regards the biotechnology industry.

The effective deployment of tax incentives must be based on an appreciation of the financial environment of today's biomedical research sector, and of how different forms of tax incentives are likely to affect these firms' investment decisions. I will first describe the current business and financial context for commercial biomedical research, and then discuss Congress' tax policy options, including ones reflected in the Lieberman-Hatch legislation,[1] to help attract private capital specifically to the discovery and development of Bioterrorism countermeasures. My conclusions are as follows.

- Notwithstanding any "structural" changes to improve the climate for private sector countermeasures research, targeted tax incentives likely will be needed to help attract private capital from other available investment opportunities.

[1] Biological, Chemical, and Radiological Weapons Countermeasures Research Act, S. 666, 108th Cong. (2003).

- Successful development of Bioterrorism countermeasures is likely to arise from both larger, profitable companies and smaller, not-yet-profitable ones. A serious deficiency in existing tax incentives for commercial biomedical research is that often they fail to convey immediate benefit to the many biomedical research companies without current income and tax liability. A countermeasures program should contain a broader range of incentives to more effectively reach all target companies.

- For more established, profitable enterprises, a program of targeted, non-refundable tax credits should provide direct and effective incentives for new countermeasures research.

- For the 95 percent of the biotechnology industry that is not-yet-profitable, more will be needed. Options include refundable tax credits that would provide a current incentive to these companies. Also, certain anti-abuse rules, such as the net operating loss limitations in Code section 382, operate to restrict tax incentives to biotech research companies relative to other industries. While these older rules are important, it is time to rethink their application to this new industry.

- Another strategy would be to provide incentives directly to the investors in smaller companies. One proposal would be to enact a reduced or zero capital gains rate for sales of countermeasures company stock. Another proposal would be to give investors a tax credit for their investments in countermeasures company stock, similar to the existing new markets tax credit. These proposals should be relatively easy to administer, and the latter proposal would provide a current benefit to investors. Another way to convey tax benefits directly to investors would be through R&D partnerships, which were curtailed in the 1980s as part of an anti-tax shelter drive. Due to their higher transaction costs, research partnerships may be less effective than other options.

II. FINANCIAL ENVIRONMENT FOR COMMERCIAL BIOMEDICAL RESEARCH

Cutting-edge commercial biomedical research takes place in a number of different settings -- from large, multinational pharmaceutical companies to start-ups focusing on one or a few technologies licensed straight from a university or other basic research institution. The importance of pharmaceutical companies in these regards should not be understated. Observers would probably agree, however, that most of the direct development work for groundbreaking biomedical therapies and diagnostics occurs in the biotechnology industry.

The biotech industry as it exists today is less than 25 years old. Presently there are about 1473 biotechnology companies in the U.S., of which over 300 are publicly traded.[2]

[2] Biotechnology Industry Organization, Biotechnology Industry Facts, *available at* http://www.bio.org/speeches/pubs/er/statistics.org (last visited October 5, 2004).

Others are better qualified than I am to describe the achievements and enormous promise of this sector of our economy, which has been called "the industry of the 21st century."

Today's biotechnology industry exhibits several striking features. First, the industry as a whole remains relatively small in financial terms. Indeed, the industry's overall annual revenues are comparable to those of a single large pharmaceutical firm. As Chart 1 shows, in 2003 U.S. biotech companies experienced aggregate revenues of about $39 billion. In contrast, the 2003 revenues of three large U.S.-based pharmaceutical companies, Johnson & Johnson, Pfizer and Merck, were $42 billion, $45 billion, and $22.5 billion respectively.

Second, while a number of established pharmaceutical companies and others are active in biotechnology research, and while there are a few relatively large, profitable biotechnology companies, most biotechnology firms are comparatively very small and do not yet have profits. In fact, there were only 60 profitable companies in the industry in 2003[3] and the biotech sector as a whole has incurred an overall financial loss every year from 1993-2003. Chart 1.

This lack of profits to date reflects the fact that, to a greater extent than other industries of which I am aware, biotech companies must engage in many years of costly research -- to demonstrate the scientific viability of their technologies, to turn them into marketable products, and to meet FDA safety and efficacy standards.

The hallmark research-intensity of biotech companies is magnified by their predominant corporate focus on the development of new medicines. Again, a comparison with the pharma industry is instructive. Whereas 2003 research and development expenditures of J&J, Pfizer and Merck averaged less than 15 percent of revenues, for the biotech industry as a whole, R&D expenditures over the last 10 years consistently have averaged about 50 percent of aggregate revenues. Chart 1.

All this research requires enormous amounts of capital. Biotech companies usually have little internally-generated cash flow to provide working capital, and since they also have few significant assets beyond their intellectual properties, they typically aren't bankable. For these reasons they must raise capital for research by repeated equity offerings, which dilute existing shareholders.

Like all other businesses, biotechnology companies must compete in the marketplace for the capital to fund their activities. Biotech firms can obtain the capital they need only if investors perceive the possibility of returns that are attractive relative to those of other available investment opportunities, given the risk involved.

Since the biotechnology business is characterized by substantial risk in the form of long lead times to product development, a continued need to raise new capital, and the real

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[3] *Resurgence: The Americas Perspective*, GLOBAL BIOTECHNOLOGY REPORT 2004 (Ernst & Young, LLP), 2004, at 21.

possibility that a research project will fail somewhere along the line, the cost of capital for the biotechnology industry is very high.

While this young and dynamic industry continues to change, these patterns seem likely to persist for some time into the future.

III. DESIGNING TAX INCENTIVES TO PROMOTE COMMERCIAL RESEARCH ON BIOTERRORISM COUNTERMEASURES.

With this financial picture of the commercial biomedical research industry in mind, let's consider what tax policy options are most likely to be effective in fostering private investment in the development of bioterrorism countermeasures.

As noted above, like other private businesses, biomedical firms must fund their research budgets by raising capital either internally, or externally from the capital markets. A private business will invest in research and development activities to the extent that expected returns cover its cost of capital for its R&D budget, taking into account risks and uncertainties of research, including losses from the inevitable failures.

In this context, a tax incentive would have the effect, directly or indirectly, of reducing the private firm's cost of marginal R&D projects (or alternatively increasing expected returns) to a level at which the investment is economically justified. As I will discuss below, one can attempt to transmit such an economic benefit through the Tax Code in various ways, with potentially quite different effects on differently situated taxpayers.

In considering the best ways to create incentives for increased biomedical R&D, the general approach taken, for example, in S. 666 -- to permit research companies to choose from a menu of different tax incentives -- seems reasonable. As we have seen, potentially successful countermeasures R&D companies find themselves in a wide variety of financial circumstances, and such a "menu" approach would permit each target company to identify the form of tax incentive that would be most effective in its own situation and that of its potential investors.

Once policymakers have determined to foster a particular commercial activity through the Tax Code, there are four key requirements in designing a successful incentive.

- Sufficient Amount. The tax benefit must be sufficient to lower the cost of a desired marginal investment to the point at which it becomes attractive to the taxpayer, given the risks and uncertainties involved. (In the case of a countermeasures incentive, even if Congress were to mitigate such structural risks as product liability, it would be necessary to offer the prospect of sufficiently compelling returns to attract private capital away from competing investment opportunities.)

- Effective Delivery. Tax incentives must be designed so that their benefit actually will flow to, and be realized by, the intended biotech companies or their investors.

- Tax Efficiency. The tax incentive should be designed so that there will be as little "leakage" as possible in the form of transaction costs such as lawyers', accountants' and promoters' fees.

- Economic Efficiency. The tax incentive should not foster economically inefficient investments the primary motivation for which is financial benefit from reducing tax expense, rather than realizing returns from economically productive activity.

It should be noted that the federal Tax Code already contains a number of incentives for commercial research. These include permitting current deduction of a broad range of research expenditures which otherwise would be required to be capitalized,[4] the tax credit for increasing research activities (the "research credit")[5] and the tax credit for clinical testing expenses for rare disease treatments (the "orphan credit").[6] Some or all of these provisions likely would apply to the activities of companies engaging in R&D on Bioterrorism countermeasures. As we will see below, however, there are serious questions whether these provisions are effective incentives for many biomedical research companies today, and consequently whether such provisions alone would induce significant new research on Bioterrorism countermeasures.

IV. TAX CREDITS FOR RESEARCH ON BIOTERRORISM COUNTERMEASURES

A tax credit operates by providing the taxpayer with a dollar-for-dollar offset to its regular federal tax liability in the amount of the credit.[7] The Code contains a number of tax credits, including some which are available for commercial research. These credits might serve as models for a countermeasures credit. The Hatch-Lieberman legislation, as discussed below, contains several proposals that are to some extent based on the following existing tax credits.

1. Research credit. Code section 41 provides a tax credit for increased research expenditures (the "research credit"). The credit applies to all industries and to all companies conducting R&D. The credit actually is comprised of three different tax credits: a regular research credit generally equal to 20 percent of the taxpayer's annual qualifying research expenditures over a base amount; an elective alternative credit set at a much lower statutory rate, yet which can provide a more favorable result in certain circumstances; and a 20 percent credit for increased payments to universities and other

[4] Code section 174.
[5] Code section 41.
[6] Code section 45C.
[7] Utilization of tax credits under existing law is subject to certain limitations. For example, the general business credit (of which the research and orphan credits are components) cannot be used to the extent that it would reduce a taxpayer's federal income tax liability below the greater of the taxpayer's tentative minimum tax or 25 percent of the taxpayer's regular tax liability in excess of $25,000. Code section 38(c)(1). Unused credits may be carried back for one taxable year or carried forward for 20 years. Code section 39.

basic research institutions. All three components of the research credit are intended to foster "incremental" research that might not occur in the absence of the tax subsidy. Available studies suggest that the research credit has been a cost effective policy tool that has perceptibly increased U.S. commercial research.[8]

Several other tax law provisions, however, operate to reduce the actual research credit benefit. Under current law, a taxpayer's R&D expenditure deductions under Code section 174 are reduced by the amount of the credit. Given a federal corporate tax rate of 35 percent, this provision has the effect of reducing the effective credit from the general 20 percent statutory rate to about 13 percent.

Further, while the research credit generally does reward companies that increase their qualifying research spending as a proportion of revenues over time, the determination of the research expenditure "base" against which increases are measured is complex, and can lead to surprising results.

- For example, a corporation might not receive a credit even though it increases its year-to-year qualifying research expenditures in absolute terms. Conversely, a company whose research expenditures are declining each year may yet receive a credit.

- In addition, the marginal rate of credit on an additional dollar of research expenditure can vary dramatically, and often is much less than the 20 percent statutory rate.

Also, the research credit provisions can appear to be generous in the case of start-up companies and other research-intensive companies which lack significant revenues and taxable income. Ironically, however, this very lack of taxable income and tax liability prevents early stage research companies from utilizing the credits.

For these reasons, the existing research credit may not be a good overall model for a countermeasures R&D tax credit.

2. Orphan credit. Code section 45C provides a different tax credit for research expenditures incurred specifically in developing so-called orphan drugs. These are treatments for serious but relatively rare diseases, and for which the marketplace alone would not provide financial returns sufficient to justify private investment. In contrast to the research credit, the orphan credit is not based on some measure of incremental research activities. Rather, the orphan credit amount is equal to a flat 50 percent of the taxpayer's annual expenditures that:

- Meet the general definition of qualified research expenditures contained in the research credit provisions of Code section 41(b); and

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[8] Gary Guenther, *CRS Report RL31181, Research Tax Credit: Policy Issues for the 107th Congress*, at n.7 (Nov. 9, 2001).

- Are incurred for human clinical trials with respect to treatments designated as orphan drugs by the Department of HHS.

3. In a manner similar to the Orphan Drug Credit, the Lieberman-Hatch legislation would add, among other credit proposals, a new section 45G to the Code which would provide a flat credit equal to 35 percent of the taxpayer's annual expenditures that:

- Qualify as research expenditures for research credit purposes under Code section 41(b); and

- Are incurred in research pursuant to a countermeasures certification by the Department of Homeland Security.

4. Tax credits can be effective in certain circumstances. Today, most commercial biotechnology research is conducted in the corporate form or in joint ventures or other collaborations among corporations. In the case of established, profitable pharmaceutical corporations and the handful of larger biotechnology companies that have current profits and income tax liability, a generous countermeasures research tax credit would provide a direct and likely effective stimulus to private sector R&D.

5. Potential limitations on the effectiveness of tax credits as incentives for countermeasures R&D. As noted earlier, most biotechnology companies do not yet have products or sales revenues, much less profits and tax liability. Exclusive reliance on a tax credit approach, therefore, would mean that for these companies there would be no current stimulus.

This situation would resemble that which obtains under current law. In this regard, in view of the overwhelmingly research-intensive character of biotech companies, it is surprising that existing Tax Code incentives are of little or no current benefit to most such companies. One economist recently has estimated that this disparate tax treatment of biotechnology raises the sector's cost of capital by almost 50 percent relative to other industries.[9]

There are some current law provisions which are intended to help preserve the value of deductions and credits for companies experiencing current losses. For example, the Code permits loss companies to carry forward net operating losses and unusable tax credits for up to 20 years. These rules are not effective in conveying the immediate incentives intended by Congress. In the case of the case of the biotech industry, where the "business model" involves up to 10 or more years of research-generated financial losses, the value of tax benefits may be speculative at best.

Further, the tough limitations on NOL and tax credit carry forwards contained in Code sections 382 and 384, which most visibly combat tax-oriented corporate mergers and acquisitions, also apply to stock ownership changes resulting from "plain vanilla" equity

[9] Kevin A. Hassett, Taxation and the Incentive to Invest in the Biotech Industry, at 4 (Apr. 15, 2003) (unpublished manuscript, on file with the American Enterprise Institute).

financings. Since such financings are the lifeblood of the biotech industry, many loss biotech companies inadvertently trigger these anti-abuse provisions and see the economic value of their tax benefit carry forwards further diminished or eliminated.

- Under these provisions, corporations must keep track of changes in holdings among their larger (5 percent or greater) stockholders. If a corporation experiences a greater than 50 percent change in ownership over any three-year period, its ability to utilize prior losses and tax credits is limited by a formula based on the (often relatively low) value of the corporation at the time of the change. These rules were aimed chiefly at the practice of profitable corporations acquiring loss corporations largely to reduce their own tax liabilities.

- Since the provisions apply to changes in stock ownership for any reason, biotech financings frequently trigger the limitations in periods when industry valuations are relatively low. Further, the so-called aggregation and segregation rules under section 382 can cause its limitations to apply to changes involving less than 5 percent shareholders, such as an initial public offering.

- While section 382 is an important anti-corporate-tax-abuse provision, it was enacted in the Tax Reform Act of 1986, before the emergence of a U.S. biotechnology industry marked by very high levels of R&D spending and consequent lengthy periods of financial losses. In certain respects, it is another example of an older tax policy which is now at odds with the business practices and needs of today's commercial research industry.

6. Preserving the value of countermeasures tax credits for biotech loss companies. One potential solution to these difficulties would be to make any new countermeasures credit refundable. A refundable tax credit would be a much more effective mechanism for delivery of the desired incentive because it would provide a current benefit regardless of whether the taxpayer had current federal taxable income and tax liability. However, some may object to refundability as an apparent use of the Tax Code to provide a direct industry subsidy.

- A variation on the concept of a refundable tax credit for new research was set out in S. 1049, introduced in the 107th Congress. This legislation would have permitted biotechnology companies with accumulated unusable NOL and research credit carryforwards to "trade them in" at a discount for a cash refund, subject to certain restrictions.

Another way to permit not-yet-profitable companies to reclaim the economic value of Bioterrorism research-related net operating losses and tax credits would be to exempt routine equity financings by certified countermeasures companies from the application of Code section 382. In this regard, S.1773/H.R. 2968, the Biotechnology Future Investment Expansion Act, would provide an exemption for equity financings to fund human clinical trials generally.

If Congress were to consider such a section 382 exemption, it would face a scope question, i.e., whether to permit the biotech company's tax benefit carryforwards to be available in the event of a future acquisition by, say, a profitable biotech or pharmaceutical company. Alternatively, it should be possible to limit a section 382 exemption so that tax loss and credit carryforwards could be utilized only by the loss biotech company itself in the event that it became successful and profitable. This more limited exemption would preserve to some extent the value of biotech companies' tax benefit carryforwards, while at the same time continuing to preclude tax-motivated corporate acquisitions in the biotech sector.

V. FAVORABLE TAX TREATMENT OF GAINS FROM STOCK IN COUNTERMEASURES RESEARCH COMPANIES

We turn now from tax incentives for countermeasures companies to incentives that would flow directly to the investors in such companies. One approach, included in the Lieberman-Hatch proposal, would be a zero tax rate on capital gains from countermeasures company stock. This proposal builds on current law as described below.

1. Current Law. Code section 1202 permits individual shareholders to exclude from income up to 50 percent of gains recognized on the disposition of small company (less than $50 million in gross assets) stock held for five years or more.

Under the capital gains tax regime enacted in 2001 and 2003, section 1202 treatment reduces the effective tax rate on gains from such "qualifying small company stock" to 14 percent. Although the otherwise applicable maximum long-term capital gains tax rate is only 15 percent, this rate is scheduled to rise as current law provisions expire, beginning in 2008.

- Alternative minimum tax provisions treating part of the excluded gain as a preference item also may offset the benefit of section 1202.

Alternatively, Code section 1045 permits shareholders to defer recognition of gains on qualifying small company stock held six months by reinvesting sale proceeds in other qualifying small company stock within sixty days. Together, sections 1202 and 1045 provide incentives for venture capital investors and lower the cost of capital for emerging companies seeking such investments.

2. The Lieberman-Hatch proposal. S. 666 would build on the provisions of section 1202 to provide a similar incentive for investment in countermeasures R&D companies. The proposal would permit individual stockholders in counter-terrorism companies with up to $750 million in gross assets to exclude 100 percent of their capital gains, and would not treat the excluded gain as an AMT preference item. The proposal also would permit corporate shareholders to exclude 50 percent of their gains on qualifying stock.

This proposal would increase the attractiveness of Bioterrorism countermeasures company stock to individual and venture capital investors. It likely would also stimulate portfolio investments by corporations in larger countermeasures companies.

- An advantage of this type of provision is that it would effectively deliver benefits regardless of whether the countermeasures company itself was profitable.

- Also, since the incentive operates by reducing or eliminating tax that would otherwise be imposed on gains, it would not require policymakers to adjust existing tax law provisions limiting the use of losses.

- There also should be low transaction costs in creating such investments.

- Finally, investors would only realize the tax benefit if the stock could in fact be sold at a gain. Generally, therefore, the taxpayer should only have to "pay" in the event that the countermeasures company is successful.

One drawback of the zero capital gains rate proposal, however, is that it does not provide a current subsidy for countermeasures research.

VI. INVESTOR TAX CREDIT FOR NEW INVESTMENT IN BIOTERRORISM COUNTERMEASURES COMPANIES.

Another strategy would be to provide a tax credit directly to investors for their acquisition of stock in countermeasures corporations. Such a credit could be based on the new markets tax credit ("NMC") contained in Code section 45D.

1. Investor credit proposal. By analogy to section 45D, the relevant provisions of a Bioterrorism investor credit might have the following features:

- The credit would be claimed by equity investors in companies engaged in certified Bioterrorism countermeasures research activities.

- The credit would be determined as a percentage of the investment.

- The credit would be spread over several years. In the case of the NMC, investors ultimately may receive credit amounts equal to almost 40 percent of the amount of their original investment.

- The entity receiving the investment would be required to use the proceeds for qualifying R&D.

- The credit would be transferable to new owners in case the original investor was to sell its stock.

- The investor's basis in its stock interest would be reduced (and any subsequent gain increased) by the amounts of credit allowed.

- The credit would be recaptured from investors in the event of that the countermeasures company were to be disqualified for any reason.

2. Some issues raised by a countermeasures investor credit proposal. Like some of the other targeted incentives we have reviewed, an investor tax credit proposal similar to the NMC would require clear definition of eligible companies and eligible activities that could be easily administered by the Internal Revenue Service. This need likely could be addressed by a certification process such as that contained in S. 666.

The NMC provisions impose an annual cap on the amount of credit-eligible investments ($1.5 billion for 2003). The Treasury Department allocates this cap among qualified community development entities whose investors then may claim the credit. For revenue estimation purposes or otherwise, a similar allocation process may make sense in the Bioterrorism countermeasures sector. If so, tax credit allocations to particular companies might be granted by the Secretary of Homeland Security as part of the certification process.

Anti-tax shelter provisions called the passive loss rules (Code section 469) generally prevent non-corporate passive investors from using tax losses and credits associated with their investments. Adapting an investor credit to the biotech sector may require loosening the application of these rules to facilitate investments by individuals.

VII. RESEARCH PARTNERSHIPS

R&D partnerships have been in the past yet another mechanism for delivering tax incentives directly to the investors in a research enterprise. S. 666 would revive these research partnerships to a limited extent. The proposal would exempt certified countermeasures R&D partnerships from the passive loss restrictions, enabling individual investors to benefit from deductions and/or credits attributable to the partnership's research spending. These changes would increase the attractiveness of investments in such partnerships to individual investors.

1. Background. Today, most biotechnology companies operate as regular business corporations taxed under "subchapter C" of the Code. As such, they are treated as separate persons for tax purposes, and determine and pay their own tax liability on the basis of their own income, expense and other items.

In contrast, partnerships (and LLCs) are not taxed as separate persons. Rather, the partnership determines its net income or loss, credits and other items, and allocates these items among its partners. Each partner generally takes its share of each item of partnership income, gain, loss deduction or credit into account on its own tax return.

Prior to the Tax Reform Act of 1986, research partnerships were in widespread use to raise capital for biomedical and other research. As the partnerships expended their capital, they generated losses which were allocated to individual investors and used to reduce their tax liabilities.

This activity was brought more or less to a halt by restrictions enacted in the 1980s, particularly the passive loss rules of Code section 469. These rules apply to individuals whose only significant participation in a partnership business is as a passive investor; and they seriously restrict the ability of such individuals to benefit from the tax losses and credits generated by passive investment.

2. Issues raised by research partnership proposals. Typically the most significant research partnership tax benefit for individual investors was their ability to deduct their share of the partnership's (normally capitalized) research expenditures that are made deductible by section 174. Since the Tax Reform Act of 1986, this benefit has been offset by the requirement that for AMT purposes individuals must amortize such amounts over a 10-year period. This AMT issue also would have to be addressed in order to make countermeasures research partnerships viable for individual investors.

There has been an issue whether countermeasures research partnerships are a tax efficient way of conveying incentives. In the past, such arrangements were characterized by relatively high transaction costs. Sponsors typically incurred significant legal and other professional fees, as well as marketing fees, which effectively reduced the value of the incentive to the research enterprise.

There have also been questions concerning the economic efficiency and tax abuse potential of research partnerships. In the 1980s Congress eliminated the tax incentives for individuals to invest in R&D partnerships, along with real estate, equipment leasing and other tax-advantaged investments, because of concerns at that time that such "tax shelters" were fostering over-investment in certain sectors, and were undermining tax compliance. The former concern, at least, might be less salient under the approach taken in S.666, since each investment in a countermeasures R&D partnership would have been subject to a prior governmental determination that investment in its proposed activities would be in the public interest.

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Tuesday, October 05, 2004

The Honorable Orrin G. Hatch
The Honorable Patrick J. Leahy
The Honorable Judd Gregg
The Honorable Edward M. Kennedy
United States Senate
Washington, DC 20510

Dear Senators:

I am writing on behalf of Teva Pharmaceuticals USA, Inc. ("Teva USA"), the largest generic drug company in the United States. Over 200 million prescriptions in the last twelve months have been filled with pharmaceuticals produced by Teva and one out of every seventeen prescriptions filled in the United States is a Teva USA product.

Teva Industries, Inc., our parent company is the world's largest generic drug company. In addition, we have built a vibrant and growing business developing and marketing innovative drugs, including one of the leading treatments for Multiple Sclerosis. Thus, we understand the scientific and business challenges faced by both innovator and generic pharmaceutical companies.

Because our parent company is based in Israel, we have a unique appreciation of the importance and gravity of the threat of terrorism in all its manifestations. We view the opportunity to contribute to preventing and defending against bioterror threats not in terms of a business strategy, but as a moral imperative.

Teva has supplied the United States government and its defense department with pharmaceuticals which are being used today to treat American forces and would likely be utilized in the event of a bioterrorist attack. In particular, we are among the worlds largest producers of anti-infectives. In recent months, Teva has been asked by the U.S. government to partner with it in the development, registration, and production of a drug used to treat leishmaniasis – a parasitic disease transmitted by the bite of some species of sand flies and often contracted by soldiers serving in Iraq. Teva willingly obliged the government's request – not because it anticipated an economic windfall, but because it was the right thing to do.

Having said this, I would like to express Teva's serious objection to certain provisions in S.666, entitled the *Biological, Chemical, and Radiological Weapons Countermeasures Research Act*, which is currently the focus of a hearing of the Health, Education, Labor and Pensions Committee and the Judiciary Committees on Wednesday. Although Teva recognizes that in some instances it may be necessary to provide additional incentives to pharmaceutical and biotechnology companies to develop bioterrorism countermeasures, Teva nevertheless has concerns that the broad, far-reaching incentives proposed in S.666, as introduced, would do far more harm than good, and that this bill has numerous loopholes and ambiguities that would be exploited to the costly detriment of the national healthcare system in countless unintended ways.

BioShield I was recently signed by the President in response to deep and well-founded concerns over this country's preparedness to handle, and ability to mitigate the devastation of, a biological terrorist attack. BioShield I created a wide variety of creative and practical measures to encourage the pharmaceutical industry to participate in preparing to thwart, and if necessary respond to, such an attack should one occur. The U.S. government has created a strong foundation with its enactment of BioShield I through entering into agreements with pharmaceutical companies for highly desirable and high profile products such as small pox vaccine, modified anthrax vaccine, and Ricin vaccine. Teva appreciates and indeed benefits from the current incentives under the Federal Food, Drug and Cosmetic Act, as well as the current R&D tax credits by undertaking research and development in the pharmaceutical arena. Given the gravity of the potential threat, Teva believes that Congress should consider extending BioShield I to include further measures that would enhance the incentives and accelerate the manufacturing of desired products. Such promising incentives that should be explored are product liability exemptions, tax credits, full research and manufacturing funding, and fast-track FDA product approval process.

Unfortunately, as introduced, S.666 does not provide the balanced and tailored incentives necessary to appropriately expand upon BioShield I's promising start. Instead, this bill includes a veritable wish-list of anti-competitive provisions long sought by the branded pharmaceutical industry even before the threat of bioterrorism arose. The impact of these provisions will have profound ramifications for the overall American healthcare system, and will dramatically increase the cost of drugs for all Americans, and for the entire range of non-terrorism related diseases and conditions.

S.666, as introduced, proposes unrestrained, expansive incentives to innovator pharmaceutical companies that are not limited to bioterrorism countermeasures. Its passage would irreparably harm the carefully crafted balance Congress created when it passed the Hatch-Waxman amendments, and strengthened those amendments just last year. This bill would also thwart the crucial goal of bringing safe, affordable generic drugs to market in a timely manner, by excessively amplifying the patent incentives for bioterror countermeasure research and development. Specifically, beyond the promising incentives outlined above, S.666 provides for a series of poorly conceived provisions of unnecessary intellectual property and market exclusivity policies:

- A two-year "wild card" patent extension that can be applied to patents and products that are wholly unrelated to any bioterrorism countermeasure, and which can be stacked, one upon another, to indefinitely delay cost-saving generic competition for drugs to treat non-bioterror related diseases and conditions;

- An additional, but greatly expanded, patent term extension opportunity, which omits the carefully balanced limitations, including unlimited patent extensions per product, of the current pharmaceutical patent term extension law;

- A doubling, on average, of the length of regulatory exclusivities for new chemical entities, supplemental new drug applications, and orphan drug products (extending each exclusivity to 10 years from 5, 3, and 7 years, respectively, under current law);

- An automatic five-year non-approval penalty against generic applicants, even if the applicant does not challenge any patents on the branded drug and does not request approval of the generic product until the brand company's patents expire.

Teva is troubled by each of these excessive and abuse-prone incentive provisions, both individually and collectively. These provisions explicitly punish the very generic drug industry that is already conducting or sponsoring studies to establish the safety and effectiveness of off-patent drugs for countermeasure purposes. The abusive patent and exclusivity provisions in S.666 would add billions of costs to the system at a time when all parties are striving to make the healthcare system more affordable.

In conclusion, Teva would like to continue to play a vital role in preparing this country to minimize any potential impact that a bioterrorist attack could inflict. However, S.666 fails to provide a workable solution to this national problem. We believe the approach offered by S. 666, as introduced, is moving in the wrong direction. Rather, we believe the better approach is to expand BioShield I to include additional incentives to further accelerate the research and manufacturing of novel countermeasure agents. We look forward to working with you and your staff on this endeavor.

Sincerely,

George Barrett
President and CEO
Teva Pharmaceuticals USA

ALAN P. TIMMINS
PRESIDENT AND CHIEF OPERATING OFFICER
AVI BIOPHARMA, INC.
PORTLAND, OREGON

TESTIMONY BEFORE THE UNITED STATES SENATE
COMMITTEE ON HEALTH, EDUCATION, LABOR, AND PENSIONS
AND
COMMITTEE ON THE JUDICIARY

JOINT HEARING

BIOSHIELD II: RESPONDING TO AN EVER-CHANGING THREAT

OCTOBER 6, 2004

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Introduction

Chairman Hatch, Chairman Gregg, Senator Leahy, Senator Kennedy, and Members of the Committee:

My name is Alan Timmins and I am the President and Chief Operating Officer of AVI BioPharma, Inc. AVI is a biotechnology company based in Oregon which was founded in 1980 on the premise that genes could be the target for drug intervention. We have developed a proprietary third generation technology, distinct from that of any of our competitors, which we focus on unmet medical needs. We have conducted 11 human clinical trials with this technology in over 300 patients and shown our technology to be safe and efficacious in cardiovascular disease and modification of drug metabolism. We are currently conducting a controlled clinical study against West Nile Virus after finding that our technology is particularly germane to the field of infectious disease, specifically including agents that are considered bioterrorism threats.

Background and Applicability

The technology also lends itself to rapid response in a therapeutic setting. This was perhaps best illustrated by an incident in mid-February at the US Army Medical Research Institute of Infection Disease (USAMRIID) located within Fort Detrick, Maryland where a researcher experienced an accidental needle stick from a syringe containing Ebola Zaire virus. Ebola is a very lethal virus, historically fatal in more than 80% of infected individuals. Upon receiving a call from scientists at USAMRIID requesting our assistance, AVI found relevant genetic sequences, synthesized two drugs, assisted USAMRIID in securing an emergency IND from the FDA, and delivered those drugs to USAMRIID within 5 days of the original request. Fortunately, throughout twenty-one days of isolation, the researcher showed no Ebola symptoms and was released at the end of that time without requiring drug intervention. The same drugs delivered to USAMRIID have now been successfully put to use in ongoing research at USAMRIID, under a Collaborative Research and Development Agreement (CRADA) between AVI and USAMRIID.

AVI has ongoing programs with outside investigators in other infectious disease areas including efforts in Marburg, Dengue, Rift Valley Fever, Crimean Congo Fever, Ricin, E coli, Yellow Fever, influenza, Hantaan virus, and SARS. Clearly, all of these diseases or infectious agents are considered to be potential bioterror threats.

In addition to efforts in these areas, we believe that we are able to currently address more than 75% of the viruses on the CDC's list of bioterror agents. Further, the lessons learned from studies involving such an array of viruses to date offer the potential to create drugs for rapid response to engineered viruses designed as bioterrorism agents.

Impact of Proposed Legislation

The issue, however, is not the capabilities of my company, or any other company, small or large, to focus on infectious diseases in general, or on bioterrorism agents specifically.

The issue is whether we will be able to bring any of this to market, for the defense of this country. This issue, therefore, depends in large measure on what you do here in terms of enacting BioShield II, and truly working to establish a biodefense industry in this country.

I have reviewed the proposals by Senators Lieberman and Hatch and offer the following comments to those proposals as they relate to smaller biotechnology companies like AVI BioPharma. As background, let me say that we are a small publicly traded biotech company that depends on the capital markets to fund our ongoing research and clinical programs. Critical to AVI, as to all small biotech companies, is our ongoing need to have favorable access to capital to fund product development, and to fund the clinical trials necessary to get those products to market.

Tax Incentives

Two of the tax incentives outlined by Senators Lieberman and Hatch will be seen as favorable by the capital markets. The R & D limited partnership structure, as proposed, would be attractive to investors because it would allow for current usage of deductions and credits by the partners, rather than only the possibility of future usage by the research organization. Also favorable to the capital market would be the capital gains incentive, because it helps to compensate investors for the perceived increase in risk that they bear with an investment in a biotechnology or biodefense company.

Patent Incentives

Similarly favorable to potential investors would be the proposed patent incentives. Though a non-cash benefit to the investor, the so called "wild card" patent extension, and related period of market exclusivity, would again be perceived as compensation for the increased risk shouldered by investors. Both the tax and patent incentives are critical to assisting in opening and maintaining the capital markets for biodefense companies.

Liability Protection

The most important incentives, however, both to the capital markets, and to the potential biodefense companies themselves are the liability protections proposed by Senators Lieberman and Hatch.

Most critical within those liability protections are the assurances of the government to the biopharma industry that the government will be a reliable, respectful, and responsible partner to biotechnology or pharmaceutical companies who join in the pursuit of bioterrorism agents. This should include guarantees that the patents and other intellectual property rights of such companies will not be "marched on" or threatened by the government, even under the stated intention of being "for the public good".

The possibilities of this occurring strikes fear in the hearts of all biotechnology or pharmaceutical executives in any company, large or small, in this country. Therefore, if strong, meaningful intellectual property protection is not extended to potential biodefense

companies, then the risk to intellectual property will be perceived as too extreme, and the best of those companies will surely not participate in any biodefense effort.

Conclusion

In conclusion, to effectively address the ongoing threat of war carried out via bioterror means, you must do the following: first, effectively implement the original BioShield procurement provisions; second, enact tax incentives for investors who fund biodefense research; third, enact patent incentives including patent extensions and periods of market exclusivity; and fourth, commit to liability protection and specifically protect the intellectual property of companies participating in biodefense, and guarantee the effectiveness of the government as a partner in the biodefense industry. These actions will pay for themselves over the long run in the quality of response from the biotechnology and pharmaceutical industries. Further, these actions will represent tremendous strides in awakening and directing the entrepreneurial spirit of the biotechnology and pharmaceutical industries toward genuine progress in biodefense. I submit to you that if fostered and appropriately channeled, this entrepreneurial spirit will prove to be the most potent weapon of all in the war against bioterrorism.

I am happy to elaborate on any of these points. Thank you very much.